DEVOTED TO RESEARCH AND CLINICAL STUDY OF THE DISEASES AND PROCESSES OF THE AGED AND AGING

Geriatrics

VOLUME 2 March - April 1947 NUMBER 2

nontoxic, nonirritating

urinary antiseptic

For treatment and prophylaxis of urinary tract infections, most gerontologists prefer a *nontoxic*, *nonirritating* antiseptic that promptly relieves pain, such as 'Caprokol' Capsules *hexylresorcinol in oil*. • Administration of 'Caprokol' Capsules produces *definitely* germicidal urine at any pH, and provides antiseptic irrigation of the urinary tract from the kidney pelvis to the urethra . . . as long as the capsules are administered. • *Nontoxic* and *nonirritating*, 'Caprokol' Capsules may be administered over long periods of time. Because of the surface analgesic effect of hexylresorcinol on the urinary tract, hematuria, burning or frequency of urination are *rarely* encountered. • Each 'Caprokol' Capsule contains 0.15 Gm. of hexylresorcinol in 25 per cent solution in a bland oil. Supplied in boxes of 25, 50 and 100 capsules. An original package of 25 capsules will be sent you promptly upon request. Sharp & Dohme, Philadelphia 1, Pa.

SHARP & DOHME

'CAPROKOL' *Capsules*

Hexylresorcinol in Oil

GERIATRICS

Official Journal of the American Geriatrics Society

EDITORIAL BOARD

A. E. HEDBACK, M.D., *Editor*

Associate Editors

EDWARD B. ALLEN, M.D., White Plains, New York

FREMONT A. CHANDLER, M.D., Chicago, Illinois

WILLIAM J. DIECKMAN, M.D., Chicago, Illinois

HAVEN EMERSON, M.D., New York City

JONATHAN FORMAN, M.D., Columbus, Ohio

GEORGE R. HERRMANN, M.D., Galveston, Texas

TREVOR H. HOWELL, M.R.C.P. Ed., Purley, Surrey, England

WINGATE M. JOHNSON, M.D., Winston-Salem, North Carolina

NORMAN JOLLIFFE, M.D., New York City

FOSTER KENNEDY, M.D., New York City

WILLIAM J. KERR, M.D., San Francisco, California

F. L. PHILIP KOCH, M.D., New York City

GEORGE W. KOSMAK, M.D., New York City

CHAUNCEY D. LEAKE, Ph.D., Galveston, Texas

OSWALD SWINNEY LOWSLEY, M.D., New York City

J. A. MYERS, M.D., Minneapolis, Minnesota

HOWARD C. NAFFZIGER, M. D., San Francisco, California

GEORGE E. PFAHLER, M.D., Philadelphia, Pennsylvania

E. A. ROVENSTINE, M.D., New York City

EDWARD A. STRECKER, M.D., Philadelphia, Pennsylvania

MALFORD W. THEWLIS, M.D., Wakefield, Rhode Island

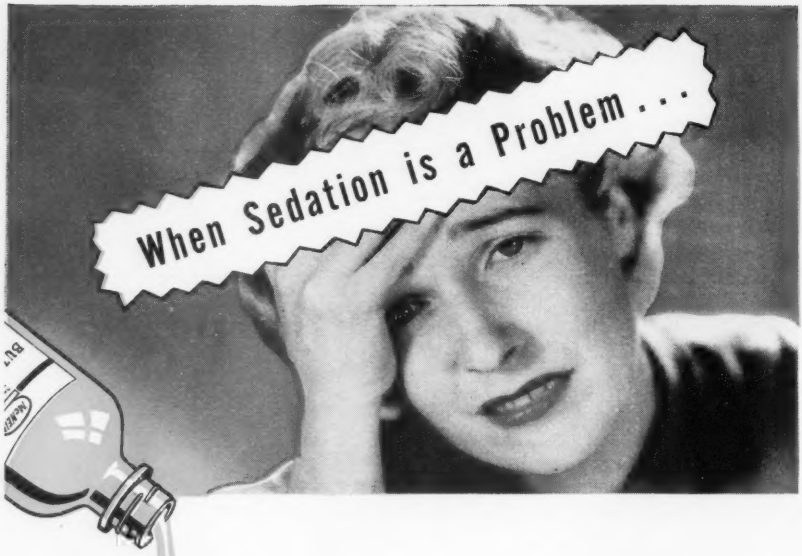
WILLARD OWEN THOMPSON, M.D., Chicago, Illinois

E. L. TUOHY, M.D., Duluth, Minnesota

WALTER E. VEST, M.D., Huntington, West Virginia

MAURICE B. VISSCHER, M.D., Minneapolis, Minnesota

S. MARX WHITE, M.D., Minneapolis, Minnesota



The very state of nervous tension, "jitters" and sleeplessness, which calls for safe, symptom-free sedation, is also apt to make the patient captious, rebellious to medication.

Elixir Butisol Sodium proves gratifyingly useful at such times. Its fresh green color, palatability and appealing flavor, help to convince the patient that something different is being done for him.

ADVANTAGES

- Intermediate duration—5 to 6 hours.
- Therapeutically effective in small dosage.
- Low toxicity—wide margin of safety.
- Inactivated in body, independent of renal excretion.
- Onset of initial effects prompt and smooth.
- Provides refreshing sleep—no lethargy or dullness on awakening.

INDICATIONS

Day-time sedation • Insomnia
Menopausal hysteria • Neuroses
Preoperative tension and apprehension
Obstetrical hypnosis

ELIXIR BUTISOL SODIUM

Contains Butisol Sodium (Sodium salt of 5-ethyl-5-secondary butyl barbituric acid "McNeil") 3 gr. per fl. oz. Supplied in bottles of one pint. Average Dosage: ½ to 1 tsp. with water. · CAUTION: Use only as directed.

Please send two trial samples of
ELIXIR BUTISOL SODIUM

Dr......

Address.....

City.....*State*.....

McNEIL
LABORATORIES, INC.
PHILADELPHIA 32 · PENNSYLVANIA, U. S. A.

GERIATRICS

Official Journal of the American Geriatrics Society

VOL. II, NO. 2 MARCH-APRIL 1947

CONTENTS

On Precursors of Gastric Carcinoma . . . . . RUDOLF SCHINDLER, M.D. 75

Anaesthesia in the Aged . . . . . E. H. WATTS, M.D. 88

The Effect of Age on the Leukocyte Count . . . . . WILLIAM R. GABBERT, M.D., LUCILE W. HUTAFF, M.D., AND GEORGE T. HARRELL, M.D. 96

Nutritional Aspects of Aging . . HENRY A. RAFSKY, M.D., F.A.C.P., AND BERNARD NEWMAN, CH.E., M.S. 101

Cutaneous Hypersensitivity Reactions to Penicillin in the Aged . . . . . JOSEPH FARRINGTON, M.D. 105

Physical Fitness and Work Capacity of Older Men . . . . . ERNST SIMONSON, M.D. 110

Editorials:

The Fear of Death 120

Preclinical Medicine and Geriatrics 121

Years as a Disability 122

Hypercholesterolemia and Artheromatous Disease in Premature Aging 123

Digests from Current Literature 127

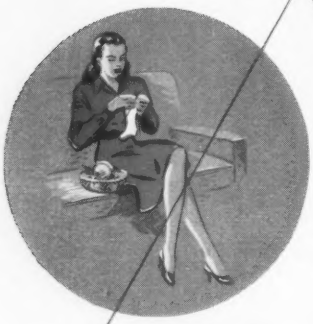
GERIATRICS is published bimonthly at Minneapolis. Publication dates: January, March, May, July, September, November. Subscription rates: $5.00 a year, $1.00 a copy; foreign, $6.00 a year, $1.20 cents a copy. Address all editorial and business correspondence to GERIATRICS, 84 South Tenth Street, Minneapolis 2, Minnesota.

ADVERTISING REPRESENTATIVES. NEW YORK 17: George Doyle, Lee Klemmer, Arthur Young, 1 East 42d Street, Suite 801, Corn Exchange Building. Telephone: Murray Hill 2-8717. CHICAGO 11: Jay H. Herz, Suite 1921, 20 North Wacker Drive. CHICAGO 6, ILL. Telephone: Central 4619. CLEVELAND 14: Bernard A. Smiler, 1125 Fidelity Building. Telephone: Main 3619. SAN FRANCISCO 4: Duncan A. Scott & Co., Mills Building. Telephone: Sutter 1393. LOS ANGELES 15: Duncan A. Scott & Co., 408 Pershing Square Building, 448 South Hill Street. Telephone: Michigan 6203.

Copyright 1946 by MODERN MEDICINE PUBLICATIONS.

Title Reg. U.S. Pat. Off. Entered as second-class matter February 14, 1946, at the post office at Minneapolis, Minnesota under the act of March 3, 1879

"Disposed" to Hypochromic Anemia . . . Nutritional Deficiency



"During growth, pregnancy and menstruation increased intake (of iron) is necessary. If any condition interferes with absorption, there will be a deficiency of iron for the manufacture of hemoglobin."*

The frequency with which in women hypochromic anemia is associated with nutritional deficiencies (promoted by finicky appetite, poor absorption, gastrointestinal upset) suggests the need for combining hemoglobin regeneration therapy with B-complex reinforcement.

Licuron-B—the bi-active antianemic—provides folic acid, choline and other B complex factors as present in liver, augmented by the crystalline vitamins thiamine, riboflavin and niacinamide.

Licuron-B acts rapidly to restore hemoglobin to normal while concurrently it raises the patient's nutritional status.

Sugar-coated tablets in bottles of 100, 500, 1000.

*Cecil, R. L.: A Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1943, pp. 965-66.

LAKESIDE LABORATORIES, INC., Milwaukee 1, Wisconsin

Licuron-B

Wisconsin Alumni Research Foundation, U. S. Pat. No. 1,877,237

ON PRECURSORS OF GASTRIC CARCINOMA

Rudolf Schindler, M.D.*

A GREAT number of people of advanced age are aware of the threat of cancer. While twenty years ago cancerphobia was almost synonymous with a morbid state of mind, nowadays health education and systematic propaganda have made non-neurotic people cancer conscious. It seems that this disease foments more fear than most other deadly diseases do. The layman has become aware of the insidious onset of the cancer symptoms; he knows that he may even be doomed without having marked symptoms. Not all forms of cancer are equally dreaded. Most dreaded by women is a carcinoma of the uterus or the breasts. Men and many women also, are afraid of having carcinoma of the stomach, the most frequent of all malignant tumors. They want to know whether they are threatened by this disease and what can be done to discover it in time. Are we able to answer these questions?

It seems that frequently carcinoma does not develop in healthy tissue (Ewing). Pathological conditions which predispose to the development of carcinoma have been called "precursors" of carcinoma. The knowledge and handling of precursors of gastric carcinoma appears an important task within the realm of geriatrics.

It has been thought that gastric carcinoma may be anteceded by one of the following three diseases: (1) Benign gastric ulcer (2) Benign gastric adenoma and (3) Chronic gastritis. The first two of these conditions in their relation to carcinoma will be discussed but briefly because either there is no true relationship (ulcer) or because the disease is of relatively minor importance (adenoma). The third condition, however, chronic gastritis, deserves thorough consideration, because its diagnosis and observation may perhaps lead to the early discovery of small symptomless gastric carcinomas.

BENIGN ULCER

The relationship between benign and carcinomatous ulcer of the stomach has been subject to much controversy. Some authors contended that 60 per cent of all benign ulcers would degenerate into malignant ones;

RUDOLF SCHINDLER, M.D., is Clinical Professor of Medicine, Gastroenterology, College of Medical Evangelists, Los Angeles, California. In 1921 he constructed the rigid Gastroscope and in 1932 the flexible type. He is author of "Gastroscopy," 1937, and "Gastritis," 1947. He was the first president of the American Gastroscopic Society. At present he is a member of numerous medical societies, including the American Gastroenterological Association, International Gastroenterological Society, and the American Gastroscopic Society.

also the other extreme opinion has found advocates—that benign ulcer never becomes malignant.

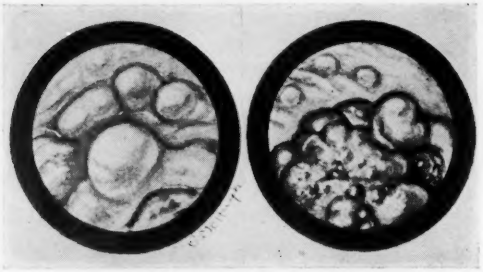
It has become more and more obvious that the static histopathologic picture alone is not able to reveal the sequence of events. Only clinical observation can find the answer. When benign gastric ulcer (proved to be present by the x-ray niche or the gastroscopic crater) is watched over any period of time, it will not develop into malignancy. In rare cases in which such development seemed to have taken place, gastroscopic examination was usually able to prove that the ulcer was malignant from the very onset. Three to 4 per cent of all adults die from gastric carcinoma, therefore, one must expect that 3 to 4 per cent of all ulcer patients also will die from accidental gastric carcinoma. That is the figure which has been accepted by many pathologists for the "malignant degeneration" of benign gastric ulcer. However, such accidental carcinomas need not necessarily develop in the ulcer area. They may originate in other portions of the stomach as well.

I have seen a few cases of duodenal and gastric ulcer in which later an accidental gastric carcinoma developed. But it seems to me that these cases are rare. I do not believe the expectancy is fulfilled, namely, that 3 to 4 out of 100 ulcer patients die from gastric carcinoma. It is amazing how rarely a true benign ulcer has been present years before the development of a gastric carcinoma. Most reluctantly I have drawn the conclusion that not only does benign ulcer not predispose to gastric carcinoma, but even that the ulcer-bearing stomach has a curiously low incidence of gastric cancer. It would appear that the ulcer-bearing stomach possesses some protective power against gastric carcinoma.

If there were a frequent transition from benign to malignant gastric ulcer, the benign ulcer in older people would have to be treated like a gastric cancer, with early resection. Since this is not so, however, conservative treatment of the benign ulcer of old age is justified. Benign ulcer is a frequent disease of the late decades of life. The first attacks usually, though not always, occur in the earlier life. Recurrences, however, continue, and it is not rare to observe ulcer relapses in the ninth decade. Therefore, the differential diagnosis of these two diseases is of the greatest practical importance. Its discussion does not belong to the domain of this article. As a rule one may state that if a patient formerly had proven benign ulcer—of the stomach or duodenum—the new gastric ulcer is most likely benign also. Exceptions do occur as mentioned before. I believe it is wise to tell the aging ulcer patient frankly that he is not threatened by gastric carcinoma any more than other people of the same age, and perhaps even less.

Benign Adenoma

Benign adenomas (often called "polyps") of the stomach are not rare. They are found at gastroscopic examinations in 2 to 4 per cent of all cases. Either one single adenoma may be seen, or several, or there may be a great number (polyposis ventriculi). Most adenomas are very small, a few millimeters only in diameter. Since they are usually soft they escape detection



(a.) (b.)

Fig. 1. *Gastric Polyposis and Carcinoma.* Gastroscopic pictures. (a) The gastric mucosa is covered with many hemispherical prominences—"polyps," benign adenomas. (b) One polyp (in the foreground) has degenerated into a polypoid carcinoma. Three benign polyps are visible in the background.

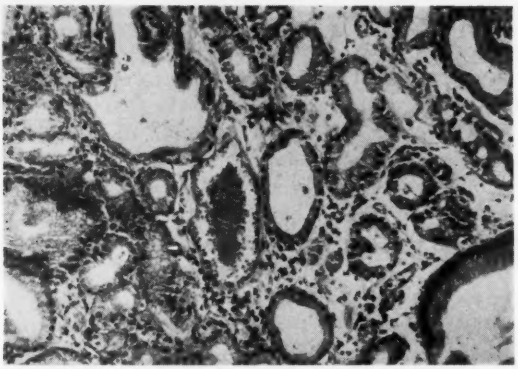


Fig. 2. *Benign Gastric Adenoma.* Microscopic section through one of the polyps shown on Fig. 1, a. Regular tubules.

at gastroscopy. The larger ones produce a round smooth filling defect on by x-ray, even with compression-relief method. They are readily recognized x-ray relief examination of the stomach. They do not often cause symptoms but occasionally may bleed, however. Hemorrhage from gastric adenoma is rare, and certainly much rarer than hemorrhage from benign submucosal tumor of the stomach.

Grier Miller has shown that gastric carcinoma may develop from benign adenoma. Undoubtedly, this tumor is a precancerous condition. (Figs. 1, 2, and 3.) It would appear, then, that each gastric polyp should be removed whenever it is discovered; yet such a procedure does not seem justified to me. The great majority of benign adenomas remain benign and never start to invade the surrounding tissue. If it would be possible to extirpate them locally as it can be done in polyps of the rectum one would not hesitate to

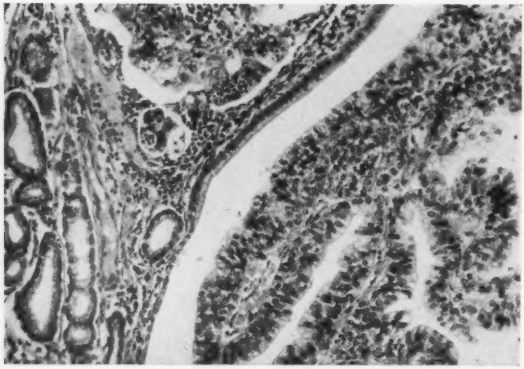


Fig. 3. *Gastric Carcinoma Developing from Benign Adenoma.* Microscopic section through the carcinoma pictured in Fig. 1, b. On the left side, there is benign looking adenomatous tissue. Center and right side show carcinoma.

do just that in every case. However, in order to remove gastric adenomas the abdomen must be opened. When this is done, small and even medium sized adenomas cannot be detected at palpation of the stomach. In large tumors local excision is possible; in small ones which cannot be found by palpation the stomach must be opened, and even then it may be impossible to discover the small tumor which in the air-distended stomach at gastroscopy had been seen so clearly; resection may become necessary. All these major procedures would be justified if a great number of benign adenomas were known to develop into carcinomas. This is not so, however, as malignant degeneration of a benign polyp is a rare exception. Therefore, only large benign adenomas with a diameter of 2 cms. and over should be extirpated as a matter of routine.

Naturally, the frequent small ones must be watched most closely and if they are seen to grow, surgery is indicated at once. This observation often is possible only by gastroscopy. As soon as a patient knows that he has a tumor he usually is willing to undergo repeat gastroscopies even if the word cancer never has been mentioned.

In cases of extensive polyposis, determining what procedure to follow can be very difficult. If the lesion is restricted to the distal portion of the stomach, especially to the antrum, resection should be advised at once. If the entire stomach is involved, so that total gastric resection would be necessary in order to remove all adenomas, careful watching is indicated. X-ray examination should be done at least every three months. Total gastric resection is too formidable a procedure to be performed without absolute necessity.

On September 9, 1939, I examined gastroscopically a 54 year old woman because of epigastric distress of 10 years duration. Multiple adenomas ("hyper-

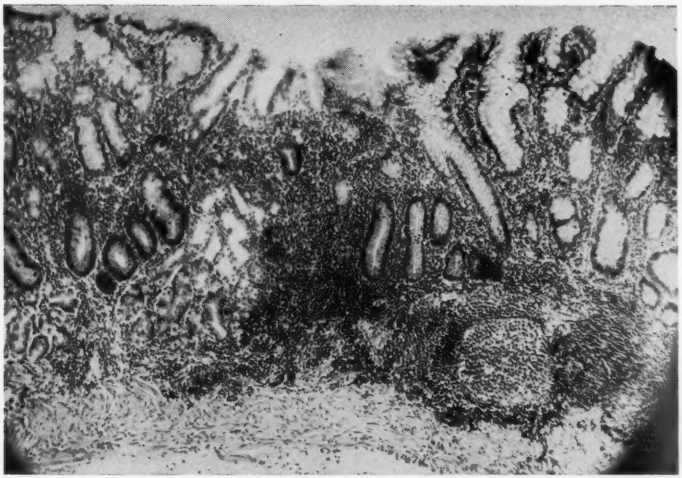


Fig. 4. *Atrophic Gastritis* (in a case of gastric carcinoma). Miscroscopic section. Only in the left lower portion of the picture a few remnants of gastric glands are seen. Most of the glands are destroyed by interstitial infiltration. The pits are proliferating. They show partly intestinal metaplasia. At the right side is an enlarged lymph follicle. The muscularis mucosae is thickened and split up. Compare this picture with the normal gastric mucosa shown on the left of Fig. 7.

plastic polyps") were found in the subcardiac region. Laparotomy was advised. The tumors could not be felt from the outside so the stomach was opened. From the inside the polyps were readily felt. They were removed digitally and the stomach was closed. No resection was done. I saw and gastroscoped the patient again on November 16, 1944, after five years. Her general condition was good. However, the polyps had recurred at the old site below the cardia, and in addition nine others had developed in the lower portions of the stomach. None looked malignant. I advised against operation and recommended continuous close observation. She presented herself again on February 3, 1947. She felt fine and had gained weight. X-ray pictures showed that the polyps had increased in number and size. Yet there was no sign of malignant degeneration. The patient realized that, if a total gastric resection would have been done in 1939, she would have been crippled unnecessarily for seven years. She decided not to have any surgery done now but to remain under close observation.

In the practical daily fight for the early discovery of gastric cancer, benign adenomas will play only a minor role.

Atrophic Gastritis

Benign ulcer and benign adenoma of the stomach are well known conditions; atrophic gastritis is not well known. Because its clinical significance is contested, a short description appears to be in order.

Although atrophic gastritis may involve the whole stomach, it is usually

Fig. 5. *Atrophic Gastritis and Carcinoma.* Miscroscopic section. The glands of the gastric mucosa are destroyed. Proliferating pits are present. Edema, interstitial infiltration and enlarged lymph follicles are seen. The carcinoma is at the right side.

most marked in its upper portions. Microscopically, three features characterize beginning atrophy (see Fig. 4) (1) Compression of the neck of the gastric glands by inflammatory exudate with formation of retention cysts. (2) Cellular infiltration immediately above the muscularis mucosae, gradually destroying the bottom of the glands. (3) Proliferation of the pits. In late stages the gastric glands are completely destroyed; within the edema and the cellular infiltration of the connective tissue only proliferating pits are seen. Their epithelium, as well as the surface epithelium, shows often a curious metaplasia, the characteristic gastric epithelium being replaced by intestinal epithelium containing a great number of goblet cells.

At gastroscopic inspection, thinning and greenish-gray discoloration of the atrophic mucosa is seen with the appearance of bluish blood vessels as soon as the atrophic changes have become marked.

Much argument exists about the clinical significance of this anatomic picture. Some authors contend that there are no symptoms at all; that abdominal and other symptoms found together with the anatomical picture of atrophic gastritis are accidental, chiefly of nervous origin, and not dependent upon the gastritis. Others admit that symptomless cases of atrophic gastritis do occur, in other cases the symptoms may subside and recur irregularly, but that existing symptoms are due to the atrophic gastritis. These symptoms, they claim, are either local or general. The local symptoms consist of epigastric pain, pressure and fullness, often combined with nausea

and vomiting. Sometimes the general symptoms dominate the disease picture, namely, spells of profound weakness and fatigue combined with anorexia and weight loss. Presence of paresthesias, numbness, tingling and sore tongue reminds of the clinical picture of pernicious anemia.

The anatomical picture, in its most severe form, is seen in most cases of pernicious anemia and in many cases of gastric carcinoma (Fig. 5). Similar pictures may be seen without these diseases. Milder patchy atrophic gastritis is not infrequent. On the whole, atrophic gastritis is a disease of advanced age, but it is not rare in earlier life. It seems that in every decade from the third decade on, there is the origin of the same number of cases; but as the individual case does not heal, there is progressive addition of cases, so that most of them are seen in the sixth decade. The total number observed decreases in the seventh decade of life, probably because there is a decrease in the number of people alive in this age group. In an analysis of 35 consecutive cases of atrophic gastritis, the following age distribution was found:

20-29 years	3 patients
30-39 years	5 patients
40-49 years	9 patients
50-59 years	10 patients
60-69 years	8 patients

As can be seen, the incidence of atrophic gastritis is highest in the cancer age; and as mentioned before, the most severe atrophic changes are often found in stomachs which contain carcinoma.

What is the relationship of these two conditions? Is their concurrent appearance of any significance? Is chronic atrophic gastritis in this age group such a frequent disease that accidental occurrence of both diseases must be expected? Or is the gastritis secondary to the carcinoma? Or finally, is the gastritis the cause of the carcinoma?

The second of these theories has been abandoned by pathologists as well as by clinicians, namely, that the gastritis is secondary to the carcinoma. The argument as to whether the concomitant occurrence is accidental or whether the gastritis is of etiologic importance for the origin of the carcinoma is not yet settled. However, it seems to me that the available evidence has started the pendulum swinging decisively in favor of a close etiologic relationship in many cases.

Staemmler expressed the thought that chronic gastritis was not more frequent in the cancer stomach than in the "normal stomach" of the same age group. He thought that one of two conclusions must be drawn: either that chronic atrophic gastritis is so frequent in advanced age that it is without significance in the development of gastric carcinoma, or that chronic atrophic gastritis is so frequent in advanced age that this very frequency

Fig. 6. *Atrophic Gastritis with Adenoma and with Carcinoma.* Microscopic section. The gastric mucosa is atrophic. It seems to be the soil of an apparently benign polyp at the right side and of a carcinoma at the left side of the picture.

would explain the great inclination of the stomach for cancer formation.

Similarly, Guiss and Stewart found signs of chronic inflammation almost regularly in cancer-bearing stomachs and in stomachs with diseases other than cancer; less frequently, but still often, in stomachs of healthy people who had died from accidents and in people who had died from extragastric cancer.

These results, however, could not be reconciled with gastroscopic examinations. Frequently people of advanced age are examined gastroscopically in whose stomach no trace of atrophic gastritis can be seen. In ulcer-bearing stomachs of people of advanced age, the stomach usually looks entirely different from the cancer-bearing stomach. The profound atrophy seen so often in cancer stomachs is almost always absent in the ulcer stomach—I observed only one case in which it was present—and often the mucosa of the ulcer-bearing stomach looks perfectly normal. It therefore must be assumed that the pathologists mentioned had disregarded the quantitative expanse of the atrophic changes. Almost every person goes through several attacks of acute gastritis during his lifetime, and after such an attack the gastric mucosa does not return to its former condition. Residues of the acute inflammation may be found in the form of some cellular infiltration and of some islands of intestinal metaplasia but such grossly invisible features are not a "disease." They cannot possibly be compared with the anatomic picture of widespread, grossly visible atrophy.

If the degree of involvement was considered, then the resuts of pathologists resembled those obtained by gastroscopists. Staut, for instance, found that the frequency of atrophic gastritis increased with age, but the

degree of involvement tended to be much greater in the cancer group than in the other groups.

Other pathologists emphasized that atrophic gastritis corresponded with precancerous conditions, recognized as such, of other organs. Ewing stated that adenoma is prone to develop in any organ which is the seat of parenchymatous atrophy. Warren and Meissner found that many of the carcinoma stomachs did not show any truly inflammatory changes. In their opinion, only the severe stage of chronic gastritis with marked epithelial alterations shows the necessary criteria for premalignancy. They thought it could be assumed that some gastric cancers arise from premalignant lesions such as true atrophic gastritis (Fig. 6).

Gastroscopic observations confirm Warren and Meissner's observation that many carcinoma-bearing stomachs do not exhibit true gastritis (Fig. 7). They are listed in the following table:

TABLE 1

CONDITION OF THE GASTRIC MUCOSA IN 48 CASES OF GASTRIC CARCINOMA

Mucosa	*Cases*
Normal	10
Superficial gastritis	8
Hypertrophic gastritis	5
Atrophic gastritis	25

In most of these cases, microscopic comparisons became possible and there was an astonishing agreement with the gastroscopic findings. If atrophic gastritis was seen, it was so extensive and severe that every comparison with other disease groups (except pernicious anemia) and with the normal stomach of advanced age had to be rejected.

The conclusion was reached that severe atrophic gastritis is so frequent in gastric carcinoma that a mere coincidence could be excluded.

These questions still remained unanswered: Does the carcinoma produce the gastritis? Or does the gastritis produce the carcinoma? Or are both diseases due to some common cause?

The first assumption was disposed of by the study of the frequency of gastritis in benign adenoma. One may understand that a decaying carcinoma might produce gastritis but it could not be understood that a pea-sized adenoma could produce gastritis. In a gastroscopic study of 1814 patients without atrophic gastritis and 353 with atrophic gastritis, benign adenomas were found to occur seven times as often in the group with gastritis than in the group without gastritis. Thus, it became obvious that atrophic gastritis precedes tumor formation.

The final proof, however, is possible only by clinical observation. If

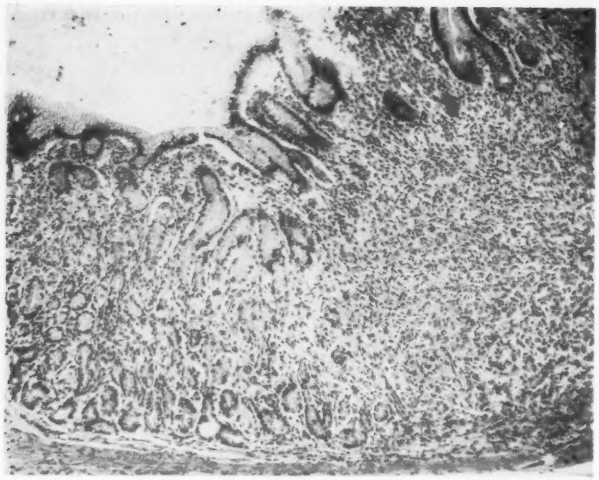


Fig. 7. *Normal Gastric Mucosa, and Gastric Carcinoma.* Microscopic section. Not every gastric carcinoma originates on the soil of atrophic gastritis. At the left side there is normal gastric mucosa without any sign of inflammation. The invading carcinoma is seen at the right side.

atrophic gastritis really is able to produce tumors in relation to its severity and the number of precancerous elements it contains, then such tumors necessarily must be most frequent in that disease which almost always is combined with most profound atrophic gastritis, namely, pernicious anemia. Recent investigation has proved that this really is so—that gastric tumors occur much more frequently in patients with pernicious anemia than in other people. In the gastroscopic study just mentioned, 15 adenomas were found in patients without atrophic gastritis (.83 per cent), 15 adenomas were found in 310 patients with uncomplicated atrophic gastritis (4.8 per cent), but six adenomas were found in 43 patients with pernicious anemia (14 per cent). The difference between the pernicious anemia patients and the patients with uncomplicated atrophic gastritis is readily explained by the dissimilar extent of the preadenomatous lesion.

For a long time it had been suspected that in pernicious anemia patients more gastric carcinomas develop than in other people. The final proof was presented in a brilliant manner by Rigler and Kaplan. They investigated 43,021 consecutive autopsies, in which 293 cases of pernicious anemia were found in persons over the age of 45. Thirty-six cases of carcinoma were present in this group—an incidence of association of 12.3 per cent. "This is over three times as great an incidence of carcinoma of the stomach as in the remainder of the same age group of the autopsy group." Later it will be

shown how spectacularly these authors used their findings in order to discover systematically small beginning carcinomas. They were not sure, however, that of all factors in pernicious anemia it was the atrophic gastritis which was responsible for the frequent carcinoma formation. If we compare the results with those of the study in benign adenomas quoted before, then it is difficult to assume that any other factor but the atrophic gastritis of pernicious anemia could have been responsible for the frequent gastric carcinomas of pernicious anemia.

Such a study is difficult in atrophic gastritis without pernicious anemia because atrophic gastritis is not a well known disease entity, readily stated at autopsy. Yet some statistics exist already which suggest strongly that chronic atrophic gastritis predisposes to gastric carcinoma.

Usland in Norway examined 125 patients in whom gastritis had been diagnosed 5 to 12 years before the study. Not less than 18 of them, 15 per cent, developed a gastric carcinoma. This figure is at least three times higher than should be expected from the law of averages.

Kapp in Switzerland analyzed 157 cases in which the diagnosis of gastritis had been made between 1915 and 1920. Twenty-one of these were treated at least five years later under the diagnosis of gastric carcinoma; in 13.4 per cent of the gastritis cases a carcinoma had developed—three times more frequently than in other people.

The only objection which can be raised against these statistics is that the diagnosis of gastritis was made without the use of the gastroscope. The fact still remains that people who suffered from some chronic stomach disease other than benign ulcer developed gastric carcinoma three times as often as other people.

Formerly, gastric carcinoma was said to develop usually in perfectly healthy people. This, however, is not true. At least one-third of all patients with gastric carcinoma suffered from some kind of epigastric distress for many years before the development of the carcinoma, and yet they had no ulcer. What other disease but chronic gastritis could have been responsible for such symptoms?

More and more cases are presented in which the sequence, atrophic gastritis—gastric carcinoma, is indubitable. Rather characteristic is the following case:

A 50-year-old male, seen in February, 1938, complained of having had indefinite gastrointestinal distress for 20 years. After a cholecystectomy in 1928 many gastric analyses revealed anacidity after histamine. There was a progressive state of weakness developing into marked exhaustion on little effort. In the last eight months more definite gastric symptoms and weight loss developed. Gastroscopy revealed a polypoid, sharply circumscribed carcinoma of the greater curvature of the antrum. There was complete atrophy of the gastric mucosa from the cardia to the pylorus. The tumor and the extensive atrophic gastritis were found in the resected specimen. The transition from atrophic gastritis tissue into tumor tissue could be seen microscopically (Fig. 8).

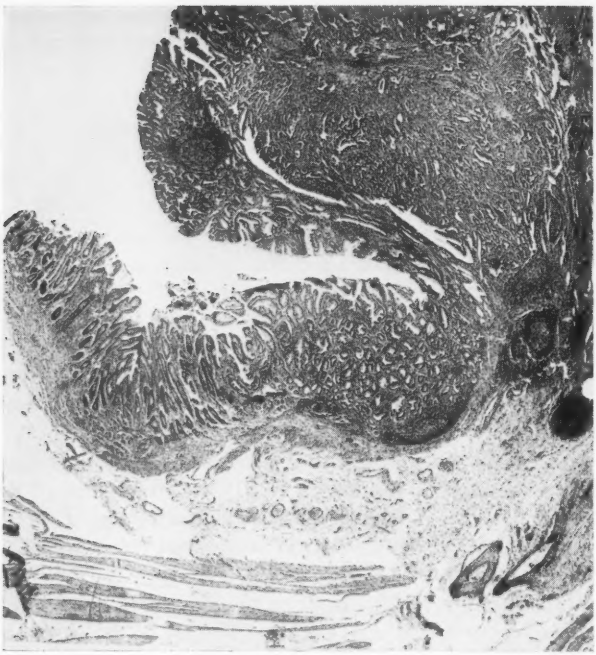


Fig. 8. *Atrophic Gastritis and Gastric Carcinoma.* Microscopic section. At the left side severe atrophic gastritis is seen. In the center there is a gradual transition into undifferentiated adenomatous tissue, from which the carcinoma originates (right side).

Thus, evidence points to the conclusion that chronic atrophic gastritis will be found to be a true and most important precursor of gastric carcinoma.

If we could watch closely the atrophic gastritis in pernicious anemia and also the uncomplicated atrophic gastritis, then we could expect to discover very small symptomless carcinomas at an early stage. A great step forward would have been made in our fight against the most frequent malignant tumor.

This has been done in an admirable manner by Rigler and Kaplan in their pernicious anemia material. They repeatedly examined by x-ray each case of pernicious anemia. Two hundred and eleven patients with pernicious anemia underwent x-ray examination; in 20 per cent only one examination was made, but in the remaining 80 per cent there were multiple examinations. Painstaking efforts were made—with constant use of gastroscopy—to reveal not only carcinoma, but also benign polyps. In the 211 cases they found 15 benign tumors (7.1 per cent) and not less than 17 carcinomas (8 per cent!). The *repeated examinations* to which these patients were sub-

jected constitute the chief reason for the attainment of so high an incidence. The ideal was fulfilled here, namely, the diagnosis of beginning symptomless carcinomas by carefully watching the recognized precancerous condition.

I am convinced that similar results could be obtained if cases of uncomplicated atrophic gastritis were watched closely.

The difficulty consists only in the discovery of chronic atrophic gastritis. This disease often causes only vague abdominal symptoms. The symptoms may be transitory and may be absent for months or even years. Only one method exists to find all possible cases of atrophic gastritis, and that is gastroscopy. It is true that histamine proved anacidity is usually a symptom of superficial—atrophic gastritis (Comfort Butsch and Eusterman; Schindler) but it occurs only in a minority of cases. In any patient in whom histamine proved anacidity was found at any time during his life, the precancerous condition of atrophic gastritis should be suspected. In order to find the highest possible amount of atrophic gastritis cases, every patient with vague and mild transient epigastric distress should be examined gastroscopically. Since gastroscopy in the hands of the well trained examiner is a harmless and quick office procedure, such a plan should present no real difficulties.

Such cases should be watched regularly, however, and given careful and repeated x-ray examination. The spot-film relief technique must be used. At least four times a year an x-ray study of the stomach relief should be undertaken.

This method may lead to the early discovery of very small and symptomless gastric carcinomas.

References

Comfort, M. W., Butsch, W. L., and Eusterman, G. B.: Observations on Gastric Acidity before and after Development of Carcinoma of the Stomach. Am. J. Dig. Dis., 4:673, 1937.

Ewing, J.: Neoplastic Diseases, 4th ed., Philadelphia: Saunders, 1940.

Guiss, L. W., and Stewart, F.: Chronic Atrophic Gastritis and Cancer of the Stomach. Arch. Surg., 46:823, 1943.

Kapp, H.: Zur Bedeutung der Anamnese des Magencarcinoms. 2. Congrès International de Gastro-Entérologie: Bruxelles, 64 Rue de la Concorde, 1937, p. 592.

Miller, T. G., Eliason, E. L., and Wright, V. W. M.: Carcinomatous Degeneration of Polyp of Stomach; Report of 8 Personal Cases with Review of 24 Recorded by Others. Arch. Int. Med., 46:841, 1930.

Rigler, L. G., and Kaplan, H. S.: Pernicious Anemia and the Early Diagnosis of Tumors of the Stomach. J. A. M. A., 128:426, 1945.

Staemmler, M.: Über Frühformen des Magencarcinoms. In Deuxième Congrès de la Société internationale de Gastro-Entérologie. Bruxelles, 64 Rue de la Concorde, 1937, p. 461.

Staut, A. P.: Gastric Mucosal Atrophy and Carcinoma of the Stomach. New York State J. Med., 45:973, 1945.

Schindler, R.: Gastritis. New York: Grune and Stratton, 1947.

Usland, O.: Über die Bedeutung der chronischen Gastritis für die Entwicklung des Magenkrebses. Acta chir. Scandinav., 76:485, 1935.

Warren, S., and Meissner, Wm. A.: Chronic Gastritis and Carcinoma of the Stomach Gastroenterology, 3:251, 1944.

ANAESTHESIA IN THE AGED

E. H. Watts, M.D.

THIS subject is one of growing importance to all anaesthetists as there are numerous factors increasing the percentage of aged and elderly patients they are called upon to anaesthetize. Baird[1] has given an excellent outline of these factors and has presented statistical data in their support. It will be sufficient here to enumerate the major factors which contribute to our increased and increasing span of life. These are: improved living conditions, marked advances in pediatrics, the steadily increasing variety of anaesthetic agents and techniques, improved surgical techniques, improved pre- and postoperative care, and last but not least, the shift in percentages resulting from the world conflict so recently ended.

The statistical evidence shows that the average life span is increasing and, as a result, an increasing number of patients require surgery, both major and minor, late in life.

The marked increase in the variety of useful anaesthetic agents has done much to widen the field of surgery for the elderly patient. The anaesthetist is now able to feel much more confident of the outcome of major surgical procedures than he was even two decades ago.

Anaesthesia has not been alone in progress. In the field of surgery new techniques and refinements of old techniques have enabled the surgeon to operate both better and faster. Unquestionably, the time factor is important where major surgery in the aged individual is concerned.

The increase in scientific knowledge regarding both pre- and postoperative supportive measures has been a very great, although all too frequently neglected factor. Data on fluid balance, haematocrit readings, blood plasma, blood serum, blood banks, and the like, have all improved the score.

Physiological Factors

In assessing the elderly patient preoperatively, it should be realized that one deals with an individual who, in varying degrees, is worn out. Further, the rate of tissue regeneration is much slower. If possible, the condition of the patient as an entity must be estimated. In so doing we require information regarding the various systems of the body. Particularly of interest is the cardiovascular system and by functional enquiry, physical examina-

ERNEST H. WATTS, M.D., is Director of Anaesthesia, University of Alberta, Canada. He is a member of the Council of the Canadian Society of Anaesthetists, Chairman of the Alberta Division of the Canadian Society of Anaesthetists and holds various posts in the Edmonton Academy of Medicine. He is also a member of the Canadian Medical Society, American Society of Anaesthetists, International Anaesthetists Research Society, and the Edmonton Academy of Medicine (and Anaesthesia).

tion and regularly by laboratory tests, we must determine the reserve of the system. We have all seen the elderly patient with a normal or somewhat lowered blood pressure, an enlarged heart having only a fair quality of heart sounds with or without murmurs, and thickened vessel walls. This, in the opinion of the author, is the picture of a poor-risk patient who some time ago was hypertensive, but who now has used up his reserve and despite the thickened vessels does not show an increased pressure. It is well known to anaesthetists how rapidly this type of patient can show severe shock.

The respiratory system has all too frequently been through several stormy sessions. The elderly patient has a somewhat fixed thoracic cage and tends to depend more on the abdominal portion of respiration. This results in a lowered respiratory exchange and predisposes to postoperative pulmonary complications. The precentage is increased, of course, if the patient has had pre-existing chronic bronchitis, bronchiectasis or asthma.

The condition of the kidneys as evidenced by the clinical and laboratory examinations is of definite importance in assessing the risk as well as in choosing the anaesthetic agent.

The frequency with which one is called upon to anaesthetize elderly patients with malignant lesions is disturbing in more ways than one. It must be remembered in considering these patients that they are shells of their former selves and now, despite seemingly good condition, have no reserve. Operative procedures which almost always are major ones cause marked shock and this must be anticipated and watched for carefully so that corrective treatment may be promptly administered.

Premedication

The usual points of consideration apply to the choice of premedication and the amount. One then must consider the general condition of the patient, the type of operation proposed, the particular surgeon and the type of anaesthesia already decided upon.

As usual one is concerned with both the physiological and psychological effects of the drug upon the patient.

It is the author's experience that short excitement periods are more frequent in patients over sixty years of age. This is perhaps explained on the basis of difficulty in controlling apprehension without getting too marked effect on the basal centres. The elderly patient rather tends to fear going to sleep due to the subconscious idea that awakening will not take place. The premedication that adequately controls this fear frequently leads to marked respiratory depression of long duration, and in turn contributes to an increased percentage of postoperative pneumonias. This delay in detoxification is of course due to the lowered metabolic function of the elderly patient. Now that rapid inductions are possible, it is advisable to choose premedication with the physiological effect predominantly in mind and not worry about having the patient too drowsy.

The question of general strength may readily trip the unwary anaesthetist who pays undue attention to the elderly patient's appearance of strength and well being. Certainly he may look well and robust and much less than his stated age, but the basal metabolic rate and resistance are lowered. The result of too heavy premedication is troublesome respiratory depression and again the old bugbear, postoperative pneumonia.

All the usual drugs of premedication may be used in suitable doses, bearing in mind certain points which must be weighed off.

Morphine—Morphine is our best analgesic and either it or one of its derivatives is required if the patient is suffering pain. To neglect this is to upset the premedication almost to the point of being useless. Morphine is, however, the greatest respiratory depressant. Normally, then, it is wise to choose light doses of morphine to avoid depression except in the presence of pain. The elderly patient should rarely have more than one-sixth of a grain of morphine and that for the more robust of the group.

Atropine — Atropine controls secretion and stimulates the basal centres, thus reducing the respiratory depression caused by morphine. It occasionally excites a patient either from idiosyncrasy or overdosage. It has no cerebral effect as far as sedation is concerned. The author prefers atropine to hyoscine in anaesthesias that are to be either avertin as a basal anaesthesia, pentothal sodium, or predominantly ether. The dose may vary up to 1/100 of a grain of atropine.

Hyoscine—Hyoscine controls secretion, stimulates the basal centres as does atropine, but in addition it produces a high degree of amnesia and as a rule has a good sedative effect. It has been suggested by several writers that this drug should in the main replace atropine. With the exceptions mentioned above the author endorses this view. The dosage may vary up to 1/150 of a grain of hyoscine.

Demerol—Demerol is a very useful drug in the premedication of elderly patients since the respiratory depression is lessened due to the atropine-like effect which it exhibits while giving sedative and analgesic effects similar to morphine. The dose may vary up to 100 mgms.

Barbiturates—The barbiturates are valuable drugs for sedation, but it must be kept in mind that they have no analgesic properties and are, as a group, respiratory depressants. It has been stated by Baird[1] that they should be omitted. At times this may well be true but one cannot make this an absolute rule. In the case of local blocks or spinal anaesthesias the safety factor contributed by a barbiturate is too valuable to be foregone since it is a well-established fact that the barbiturates markedly raise the minimum lethal dose of local anaesthetic drugs. Over and above these special cases, the author is more inclined, as a rule, to lower the doses of other premedicative drugs and use the barbiturates. For the local anaesthetic group it is wise to markedly decrease doses of morphine and increase

the dose of the barbiturate. A maximum does of barbiturate for the elderly patient would be a grain and one-half of nembutal or a comparable dose of other selected drugs.

The Choice of Agents

Fortunately, the field widens fairly steadily and with each addition to our armamentarium we are enabled to choose varying combinations of agents for specific purposes. Let us deal specifically with the standard agents in use.

Chloroform—Aside from the truth of the statement that the part time anaesthetist should use the agent with which he is most familiar, even if it should be chloroform, it is difficult to visualize an indication for the use of chloroform in the elderly patient. One assumes, of course, the availability of modern agents and apparatus. It is granted that the country practitioner may be forced to use choloroform on an elderly patient in a farmhouse, but he must not delude himself that he has not thereby increased the risk to the patient.

Ether—Ether has been a useful agent in the past and, for that matter, is a widely used and valuable agent of the present. However, its field of usefulness in the elderly patient is steadily decreasing since we now have other agents from which to choose that do not involve the metabolic imbalance or the irritation of liver, lungs and kidneys produced by ether.

Nitrous Oxide—This agent is useful for minor surgery but one must ever be alert for anoxaemia which develops so easily and does a great deal of harm to the patient.

Cyclopropane—In cyclopropane we have a most useful and excellent agent. It has rapid and smooth induction and recovery periods, produces excellent relaxation and allows the use of very high oxygen concentrations. Cyclopropane is probably the most widely used of all the agents for the elderly patient, and most anaesthetists tend to choose this agent for their poor-risk patients.

In some reported series the mortality rate is highest with this agent. At first glance this is discouraging but one must read further to get the true picture. One finds that cyclopropane has been, as stated above, the agent of choice for the desperately ill patients. Hershey and Rovenstine[2] have shown that cyclopropane is an excellent agent for use in the presence of severe hemorrhage. This is most interesting in view of the frequent complaints that cyclopropane increases bleeding during the operation.

Pentothal Sodium—This short acting barbiturate which is administered intravenously has come rapidly to the fore in an ever-widening field.

The use of pentothal sodium intravenously, supplemented by nitrous oxide and oxygen in analgesic doses varying between 50-50 per cent and 75-25 per cent, has proved to be a useful and excellent combination for a wide variety of cases.

Age and shock have been given as contra-indications but the report of Adams and Gray[3] does not bear this out. Their report brings attention to several pertinent points. In the first place, these patients require supportive measures. It is manifestly unfair to blame the poor result when supportive measures were withheld upon the anaesthetic agent. Again, many difficulties from respiratory depression are not so much due to the agent as they are to the faulty technique or knowledge of the man behind the syringe. In the aged patient dosage should be initially very small and supplemented with small fractional doses, repeated more frequently if necessary. If this procedure is followed, respiratory depression will not be a cause for concern and pentothal sodium will be an excellent choice.

Curare—Thanks to Griffith[7] this erstwhile fatally poisonous drug is now, in controlled doses, one of the greatest boons to the anaesthetist to date. Since it provides muscular relaxation and bowel contraction comparable to that achieved with spinal anaesthesia, it has simplified anaesthesia in the debilitated elderly patient.

Spinal Anaesthesia

This type of anaesthesia has, after a rather rough passage, been steadily increasing in popularity due primarily to the use of less toxic drugs and, secondarily, to the introduction of continuous spinal anaesthesia by Lemmon[4].

Procain has long been the standby and measuring gauge of spinal anaesthesia. Other drugs are listed as more or less toxic than procain, or as having a longer or shorter action. Of the newer drugs in use, three in particular will be discussed. The first one is pontocain. The statement has been made that pontocain is more toxic than procain. This indeed is true weight for weight, but in the dosages used for spinal anaesthesia the weights are not equal since, by weight, doses vary from a tenth to a twentieth of the weight of procain ordinarily used for a similar spinal anaesthesia. It is the author's opinion that in this dosage pontocain is definitely less toxic and at the same time gives longer lasting anaesthesia.

The second drug is metycain. This agent is given in similar doses to procain as far as weight is concerned but, again, has a definite factor of increased duration of anaesthesia and is probably somewhat less toxic as well.

The third drug is Nupercain. Once again, weight for weight, this is an exceedingly toxic drug as compared to procain. However, on a clinical dosage basis the facts are reversed since doses are so small. It is used in two concentrations, a light and a heavy solution, or in a combination of the two. The light solution is used in doses up to 20 cc. of the 1-1500 solution. (13.3 mgms.) of nupercain while the light solution is used in doses up to 2 cc. of a 1-200 solution (10 mgms.) of nupercain.

With the advent of continuous spinal anaesthesia the value of the tech-

nique in the elderly patient has been markedly increased. Once again proper supportive measures are likely to be required and with their use a more rational point of view is established as to the use of spinal anaesthesia.

This technique described by Lemmon[4] offers three main advantages: First, the necessity of working against time is readily eliminated; if more time is required, additional doses are given. Secondly, the dosage is easily made to conform to the case. This is particularly useful in the cases where one cannot, in the beginning, know whether a long or short time will be required; for example, a diagnostic laparotomy in the case of carcinoma of the stomach may be merely an open and close procedure if the secondaries are widespread, or it may involve a long gastric resection. Thirdly, the dosage need never be high at any given time. Reports are on record in which massive doses have been used in the early minutes of a continuous spinal. However, one of the main advantages has been completely lost by doing this. The usefulness of spinal anaesthesia is increased by this latter factor as far as the elderly patient is concerned. One can avoid the initial massive dosage of single administration spinals which result in high absorption of the drug and reactions. The patient need never have a large amount of the drug to detoxify at any time.

Continuous Caudal Analgesia

This technique has been described by Hingson and Edwards[5]. It is perhaps too early to properly assess this technique but it has these points to recommend its use: low dosage at any given time and the ablity to re-administer a required dose.

It is often technically difficult, however, to insert the needle without trauma in the aged patient. The dosage in total is necessarily higher than with spinal analgesia and the number of toxic effects is increased.

Refrigeration Anaesthesia

This technique described by Allen[6] is interesting and useful. It is time-consuming, and careful attention to detail is essential. Again, experience is not great enough to assess either its real value or its place in anaesthesia. The few cases in which I have used it point to a real value in the aged patient.

Special Techniques

It may be of value to mention some of the techniques used for specific procedures.

(*a*) *Fractured neck of femur.* One of the commonly occurring and usually shocking accidents to aged patients is a fractured neck of the femur. Every movement of these patients causes shock to increase, due to the pain stimuli. Several different techniques have been used for this group. Some years ago they were anaesthetized with nitrous oxide. Due to the cyanosis or, in any event, to the degree of anoxaemia almost always present, this

technique was first modified by the additions of small volumes of ether, thus allowing increased oxygenation. Finally the technique was discarded in favour of other ones. The next method was the use of cyclopropane. This was an excellent method from an anaesthetic viewpoint but was discarded due to the possible explosion hazard, since x-ray plates are usually required as the reduction and pinning proceed.

A change was made to local anaesthesia. An intracapsular block using 20 to 30 cc. of 2 per cent novocain was done followed by local infiltration of the line of incision and down to the periosteum. This method was in itself only fairly successful due to an unexpected reason. Following the block, the patient was comfortable during the reduction of the fracture, but when the patient's legs were postured in wide adduction, definite discomfort was caused by pain from stretching the adductor muscles, especially in the good leg. The next moves were in fairly rapid succession. Analgesic doses of nitrous oxide and oxygen were begun before or after the above mentioned block to relieve the discomfort of posture, then small doses of pentothal were used for the same purpose.

The final move has been to anaesthetize the patient in bed or on the stretcher with pentothal to avoid the pain of being moved. Once on the table, pentothal sodium is again begun and continued in small fractional doses supplemented by nitrous oxide and oxygen. This technique has been very successful and is less time-consuming than the local blocks.

(*b*) *Prostatectomy*—The older two-stage operation is usually handled as follows: for the first stage, either spinal anaesthesia using small doses of pontocain or cyclopropane has been the choice; for the second stage, either cyclopropane or pentothal sodium and analgesic doses of nitrous oxide and oxygen has been the choice. For the newer transurethral resection, the choice has been either spinal anaesthesia, pentothal sodium or continuous caudal analgesia.

(*c*) *Intra-abdominal surgery*—The advent of continuous spinal anaesthesia has marked an increase in the amount of spinal anaesthesia used for aged patients. This may be supplemented with analgesic doses of nitrous oxide or light anaesthetic doses of cyclopropane. The results have been very satisfactory to all concerned, that is, the patient, the surgeon and the anaesthetist.

In the very debilitated patient, even continuous spinal anaesthesia is not to be considered. In this situation either cyclopropane and curare as first described by Griffith[7] or the interesting combination recently put forward by Knight[8] of pentothal, curare and nitrous oxide will provide very satisfactory operating conditions for the surgeon, a wider margin of safety for the patient and more peace of mind for the anaesthetist. These combinations are so satisfactory that they are reducing quite markedly the risk of operating on elderly patients.

(*d*) *Ophthalmic Surgery*—The use of the pentothal sodium and nitrous oxide combination in the field of ophthalmic surgery for the extraction of senile cataracts has been very satisfactory and will form the basis of a paper to be published shortly.

SUMMARY

The increasing need for thought and study of the problem of anaesthesia in the aged has been presented.

The problem of physiological changes due to age has been reviewed.

Drugs for premedication have been assessed.

The choice of anaesthetic agents has been given.

A few general techniques have been outlined.

REFERENCES

1. BAIRD, J. W.: Geriatrics and anaesthesia, Anaesthesiology, 4: 17, 1943.
2. HERSHEY, S. G. and ROVENSTINE, E. A.: Value of cyclopropane in anaesthetic management of patients with recent severe haemorrhage, Anaesthesiology, 5: 149, 1944.
3. ADAM, R. C. and GRAY, H. K.: Intravenous anaesthesia with pentothal sodium in gunshot wound associated with accompanying severe traumatic shock and loss of blood, Anaesthesiology, 4: 70, 1943.
4. LEMMON, W. T.: Method for continuous spinal anaesthesia, Ann. Surg., 111: 141, 1940.
5. HINGSON, R. A. and EDWARDS, W. D.: Continuous caudal analgesia, J. Am. M. Ass., 123: 538, 1943.
6. ALLEN, F. M.: Refrigeration anaesthesia for limb operations, Anaesthesiology, 4: 12, 1943.
7. GRIFFITH, H. R., and JOHNSON, G. E.: The use of curare in general anaesthesia. Anaesthesiology 3: 418 (July) 1942.
8. KNIGHT, R. T.: Combined Use of Sodium Pentothal, Curare, Nitrous Oxide. C. M. A. J. 55: 356-360, 1946.

A STUDY OF LATER MATURITY

A LONG-TERM study of social adjustment in later maturity has recently been started by three members of the faculty of the University of Chicago; Ernest W. Burgess, Professor of Sociology, Robert J. Havighurst, Professor of Education, and Herbert Goldhamer, Assistant Professor of Sociology.

It is the intention of the study to make a systematic and comprehensive analysis of the social and personal adjustment of older adults. As the principal group to be studied, it is proposed to enroll 2,000 persons, men and women between the ages of 50 and 60. Present plans are to follow the careers of these people as long as they may live, and to secure data from them as they pass from later maturity to old age. Persons participating in this study will be asked to fill out a detailed questionnaire and to give one interview to a staff member each year.

This study is analogous to the longitudinal studies of childhood and adolescence which have been conducted by several research groups within the past two decades. However, a longitudinal study of adults and older people will present problems of method and interpretation quite different from the problems of conducting such a study with children.

The cooperating study group will be drawn largely, if not entirely, from Greater Chicago. From this area, a fairly good cross-section of economic and religious groups can be selected.

From *University of Chicago Committee on Human Development*

THE EFFECT OF AGE ON THE LEUKOCYTE COUNT

A Comparison of White Blood Cell Counts in Aged and Young Individuals, with Special Reference to the Response to Infection.

William R. Gabbert, M.D., Lucile W. Hutaff, M.D. and George T. Harrell, M.D.

WITH increasing interest in the field of geriatrics the need of standards for elderly people in health and disease has become recognized. Very little work has been done, however, to determine the "average" or "normal" hematologic values in old age, or to analyze the response of the blood in aged individuals to the demands of an infectious process. Several investigations have been devoted primarily to studies of the erythrocytes in older people,[1] but very little has been noted concerning the leukocytes.

The leukocyte count in normal adults, according to Wintrobe,[2] is 5,000 to 10,000 cells per cubic millimeter, the average being 7,000. No further age or sex distinction is made either by Wintrobe or by other textbook authors. In an article by Newman and Gitlow the total leukocyte counts and differential counts in a group of 50 normal males and 50 normal females of 65 years or over were reported[3]. These authors concluded that the accepted standards for the total leukocyte count may be applied to aged individuals. There was a slight difference between the total leukocyte counts in men and those in women, the women averaging 8,170 and the men 8,330. Miller studied the leukocyte counts in 160 men past the age of 60 years, and found the mean count to be 7,700 per cubic millimeter[4]. In 95 per cent of the cases, the counts ranged from 4,000 to 13,000 white blood cells per cubic millimeter.

It might be assumed that, since aging leads to degeneration in other systems of the body—for instance, the neurologic and the vascular systems—a similar "wearing out" process may take place in the bone marrow, thus interfering with the ability of the patient to combat infection. The present study was undertaken to confirm or refute this assumption by com-

WILLIAM R. GABBERT, M.D., Massachusetts Memorial Hospital, Boston, is a graduate of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, North Carolina.

LUCILE W. HUTAFF, M.D., is Instructor in Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, North Carolina, in which city she holds several hospital appointments.

GEORGE T. HARRELL, JR., M.D., is Professor of Medicine, Bowman Gray School of Medicine of Wake Forest College, and Director of the Department of Internal Medicine; Chairman, Section on Medical Education, Southern Medical Association; member, Editorial Committee, *Journal of Clinical Investigation.*

paring the variability of the white blood cell count in young and old individuals, and especially the leukocyte response to infection.

Material and Method

The records of 1,004 consecutive hospital patients, aged 20 years or over, who were seen on the medical, obstetric, or surgical services of the North Carolina Baptist Hospital between May, 1944, and November, 1945, were reviewed. For reasons stated below, only 836 records were used for this study. For the purpose of this investigation, the patients were classified as "infected" or "non-infected." Pregnant women were not included, because pregnancy is known to cause physiologic leukocytosis; the classification of these cases in the "non-infected" group would obviously produce an abnormally high average white blood cell count for younger individuals. All primary blood dyscrasias, such as leukemia and granulocytopenia, were discarded.

The criteria used for classifying patients as "infected" or "non-infected" were: the clinical impression on admission to the hospital, the oral temperature on admission, and the final diagnosis. The following diagnoses, which were usually incidental, did not serve to place a patient in the "infected" group unless the oral temperature on admission was higher than 100° F.: chronic sinusitis, benign prostatic hypertrophy, chronic cholecystitis, chronic bursitis, and chronic cervicitis. A few conditions of non-infectious nature in which leukocytosis usually occurs were classed in the 'infected" group. These conditions included burns, cerebral hemorrhage, and coronary occlusion. Division of the "infected" cases into acute and chronic types was found to be impractical.

The total leukocyte counts were determined by graduate or student technicians in the clinical hematology laboratory, or by junior and senior medical students acting as clinical clerks. Only the initial white blood cell count was considered. The Spencer Bright Line Haemocytometer and clinical pipettes were used.

The 'infected" and the "non-infected" groups were divided according to age; the average white blood cell count for each decade was calculated in both groups, and the results were compared by statistical methods[5].

Results

The results of this study are summarized in tables 1 and 2. Table 4 compares the findings in the "non-infected" patients with those obtained in a group of "healthy" adults working in the same community.[6] Tables 3, 5, and 6 compare the mean values for the younger and older age groups in both the "non-infected" patients and the "healthy" adults.

An attempt was made to compare the differential counts in the "non-infected" and "infected" hospital patients but it was found that when only 100 leukocytes were counted the percentages were so unreliable that such a comparison was of no value.

TABLE 1.

ADMISSION WHITE BLOOD CELL COUNTS IN "NON-INFECTED" HOSPITAL PATIENTS BY DECADES

Age (years)	Total Cases	Range (cells/cu. mm.)	True Mean	Standard Deviation	Variation
20-29	92	2,000-16,000	8,281	2,056	24.8
30-39	167	4,000-16,000	8,364	2,316	27.7
40-49	156	2,000-16,000	8,102	2,494	30.8
50-59	134	2,000-14,000	6,089*	2,274	37.3
60-69	100	2,000-16,000	7,919	2,216	27.9
70-	45	2,000-16,000	8,377	2,108	25.2
Total	694	2,000-16,000	7,816	2,140	23.8

1. All statistical calculations in all the tables were made according to methods advocated by Chambers[5].

*The mean for patients of this age is by statistical calculation significantly lower than the means for the 40-49 year age group and the 60-69 year age group. The interpretation of this finding is not clear.

TABLE 2.

ADMISSION WHITE BLOOD CELL COUNTS IN "INFECTED" HOSPITAL PATIENTS BY DECADES

Age (years)	Total Cases	Range (cells/cu. mm.)	True Mean	Standard Deviation	Variation
20-29	37	4,000-28,000	13,215	5,462	41.5
30-39	30	4,000-26,000	11,799	3,410	28.9
40-49	30	4,000-28,000	11,799	5,230	44.3
50-59	22	6,000-22,000	11,727	4,024	34.3
60-69	13	6,000-20,000	12,076	3,646	30.2
70-	10	4,000-28,000	14,799	5,400	36.5
Total	142	4,000-28,000	12,337	4,620	25.5

DISCUSSION OF RESULTS

In the "non-infected" group (table 1) the means obtained for the various decades varied so little that in only one case was a difference twice that of standard error approached. The average white cell counts for all ages ranged between 6,089 and 8,377. In this series there was no significant difference between the mean white blood cell count in patients 20 to 49 years old and that in patients of 50 years and over.

In the "infected" patients (table 2) the mean white blood cell count for each age group was higher than the comparable mean white blood cell count in the "non-infected" patients. The variation among the means obtained for the various decades was considerably greater in the "infected" group than in the "non-infected" class, but the mean white blood cell count in the 20-49 year age group of "infected" patients did not differ significantly from that in the group 50 years and over.

TABLE 3.

COMPARISON OF MEAN ADMISSION LEUKOCYTE COUNTS IN THE YOUNGER AND OLDER AGE GROUPS OF HOSPITAL PATIENTS

	Age (years)	Number Cases	True Mean (cells/cu. mm.)	Standard Deviation	Statistical Significance
"Non-Infected" Patients	20-49	415	8277	2342	$\frac{\text{Difference}}{\text{Standard Error of Diff.}} = 0.392^*$
	50-	279	7988	2272	
"Infected" Patients	20-49	97	12669	4912	$\frac{\text{Difference}}{\text{Standard Error of Diff.}} = 0.109^*$
	50-	45	12775	2287	

* $\frac{\text{Difference}}{\text{Standard Error of Difference}}$ of less than 2.0 is not considered to be significant.

TABLE 4.

COMPARISON OF MEAN ADMISSION LEUKOCYTE COUNTS AT VARIOUS AGES IN "NON-INFECTED" PATIENTS AND "HEALTHY" ADULTS WORKING IN THE SAME LOCALITY

	"Non-Infected" Hospital Patients				"Healthy" Working Adults[6]			
Age (years)	Number Cases	True Mean (cells/cu. mm.)	Standard Deviation	Variation	Number Cases	True Mean (cells/cu. mm.)	Standard Deviation	Variation
20-29	92	8281	2056	24.8	651	8719	2229	25.4
30-39	167	8364	2316	27.7	491	8319	2287	25.7
40-49	156	8102	2494	30.8	271	8824	2146	24.3
50-59	134	6089	2274	37.3	87	8511	2282	26.8
60-69	100	7919	2216	27.9	0			
70-	45	8377	2108	25.2	0			
Total	694	7816*	2140	23.8	1500	8807*	2228	25.2

*Comparison of the mean for each group shows that $\frac{\text{Difference}}{\text{Standard Error of Difference}} = 9.96$; this is a statistically significant difference.

TABLE 6.

COMPARISON OF MEN ADMISSION LEUKOCYTE COUNTS OF "NON-INFECTED" HOSPITAL PATIENTS WITH THE MEAN LEUKOCYTE COUNTS OF "HEALTHY" ADULTS OF THE SAME AGE GROUP

		Number Cases	True Mean (cells/cu. mm.)	Standard Deviation	Statistical Significance
20-49 Years	Hospital Patients	415	8277	2342	$\frac{\text{Difference}}{\text{Standard Error of Diff.}} = 0.920^{**}$
	Healthy Adults	1413	8825	2223	
50 Years and Over	Hospital Patients	279	7988	2272	$\frac{\text{Difference}}{\text{Standard Error of Diff.}} = 0.523^{**}$
	Healthy Adults	87*	8511	2282	

*All patients in this group are from 50 to 59 years old.

** $\frac{\text{Difference}}{\text{Standard Error of Difference}}$ of less than 2.0 is not considered to be significant.

TABLE 5.

COMPARISON OF MEAN LEUKOCYTE COUNTS IN THE YOUNGER AND OLDER AGE GROUPS "HEALTHY" WORKING ADULTS

Age (years)	Number Cases	True Mean (cells/cu. mm.)	Standard Deviation	Statistical Significance
20-49	1413	8825	2223	$\frac{\text{Difference}}{\text{Standard Error of Diff.}} = 1.24^*$
50-59	87	8511	2287	

* $\frac{\text{Difference}}{\text{Standard Error of Difference}}$ of less than 2.0 is not considered to be significant.

SUMMARY AND CONCLUSIONS

1. In a study of 836 adult hospital patients, the mean white blood cell count in the older age group (50 years and over) was not found to differ significantly from the mean white blood cell count in the younger age group (20-49 years).

2. The response to infection was comparable in all decades.

3. According to statistical calculations, the white blood cell counts in the hospitalized "non-infected" patients in the younger and older age groups were significantly higher than the white blood cell counts in a group of "healthy" individuals working in the same locality; this finding was interpreted as having no clinical importance.

BIBLIOGRAPHY

1. NEWMAN, B., and GITLOW, S.: Blood Studies in the Aged: The Erythrocyte in the Aged Male and Female. Am. J. M. Sc., 205:677-687 (May), 1943.
2. WINTROBE, M. M.: Clinical Hematology, ed. 2, Philadelphia, Lea and Febiger, 1946, p. 159.
3. NEWMAN, B., and GITLOW, S.: Blood Studies in the Aged: Part II. The Leukocytes in the Aged Male and Female. Am. J. M. Sc., 206:622-625 (Nov.), 1943.
4. MILLER, I.: Normal Hematologic Standards in the Aged. J. Lab. & Clin. Med., 24:1172-1176 (Aug.), 1939.
5. CHAMBERS, E. G.: Statistical Calculation for Beginners, Cambridge, University Press, 1940.
6. HUTAFF, L., and HARRELL, G. T.: An Analysis of Blood Counts of 1740 "Healthy" North Carolinians. No. Car. M. J., 7:641-645 (Dec.) 1946.

OLDEST PRACTICING PHYSICIAN CONTEST

Dr. George D. Haggard of Minneapolis, Minnesota, is believed to be the oldest practicing physician in the country.

Dr. Haggard observed his 90th birthday on January 18 of this year, and has been in active practice for almost 54 years.

Geriatrics invites correspondence in order to ascertain whether Dr. Haggard has established the record of being the oldest in the profession in active practice.

NUTRITIONAL ASPECTS OF AGING

Henry A. Rafsky, M.D., F.A.C.P
and Bernard Newman, CH.E., M.S.

IN PREVIOUS articles it was shown that in apparently normal aged individuals there is a tendency, in general, to low blood levels and excretions of thiamin,[1] low blood levels and high tolerance to ascorbic acid,[2] and a high incidence of porphyrinuria[3] which could be made to disappear upon the oral administration of nicotinic acid.[4] It was likewise demonstrated that in a large percentage of apparently healthy individuals past the age of sixty-five years, the blood levels of carotene and vitamin A were subnormal.[5]

Various explanations may be offered for these findings: (1) The diets were lacking in specific vitamins (2) There was inadequate intake of food (3) The vitamins were not absorbed in sufficient amounts from the intestinal tract (4) Failure of the organism to store sufficient amounts of the vitamins in the liver or other storage depots of the body to maintain adequate blood levels or, as may be the case with carotene and vitamin A, the latter not being synthesized at a normal rate from the carotene that is ingested along with the food.

So far as the first of the above-mentioned possibilities is concerned, a chemical analysis of the diets of a series of experimental subjects during seven consecutive days showed that the food contained an ample supply of vitamins according to the standards of the National Research Council.* These findings may be seen in Table 1. In order to determine whether or not there was a sufficient amount of food being ingested, the quantity of each of the dietary constituents was carefully measured and weighed for seven consecutive twenty-four-hour periods, and the intake of protein, fat, carbohydrate, and the total caloric intake were computed from these values.[6] These results are to be more fully discussed in a subsequent paper. However, as may be seen in Table 2, where we have cited the average results found for an experimental group of 65 normal individuals past the age of 65 years, the intake was adequate, both for the protein and for the total daily caloric value. Hence, the factor of inadequate intake may be ruled

---

HARRY A. RAFSKY, M.D., New York City, is Attending Gastroenterologist at Beth Israel Hospital, Gastroenterologist at Lenox Hill Hospital, and Consultant Gastroenterologist at Rockaway Beach Hospital and Dispensary.

BERNARD NEWMAN, Ch. E., M.S., is Director of Chemical Laboratories, Hospital of Daughters of Jacob, New York City. He is a member of the New York Academy of Sciences American Public Health Association, and the American-Societ Medical Society.

THE vitamin analyses of the diets were performed by Dr. S. H. Rubin, Nutley, N. J.

This study was aided by a grant from Hoffmann-La Roche, Inc., Nutley, N. J.

TABLE 1.

	B_1	B_2	C	Fe	Niacin	Carotene	Vitamin A
1st 24-hr.	0.88	0.97	59	5.6	11.6	6,000	2,700
2nd 24-hr.	0.83	1.33	16	10.0	10.4	11,400	1,900
3rd 24-hr.	1.11	1.78	117	3.7	13.1	11,800	1,900
4th 24-hr.	0.84	1.22	16	9.0	6.9	2,100	1,300
5th 24-hr.	0.70	1.29	18	2.5	8.6	8,800	1,300
6th 24-hr.	0.51	1.03	40	10.9	10.6	1,500	1,500

Note: 24-hr. values are in mgm. per diem, except Carotene and Vitamin A, which are in U.S.P. units per diem.

out as a possible cause for the tendency to avitaminosis, or to what may be termed "biochemical avitaminosis" in the aged.

The third item, namely a lack of assimilation or absorption of the vitamins which have been ingested, was also investigated. In studying the tolerance of normal aged individuals to orally administered vitamin A,[7] it was found that a rise in the serum levels does occur after such administration. Similar findings were observed for thiamin,[1] nicotinic acid,[4] and

TABLE 2.

Gms.	Range	Mean
Protein	66-97.4	83.4
Fat	44.8-68.3	58.9
Carbohyd.	203.2-286.4	244.7
Total Cal.	1604-2260	1843

for ascorbic acid.[2] In other words, it may be concluded that relatively normal rates of assimilation and absorption of these vitamins takes place in normal aged subjects.

The last of the four above-mentioned factors, the question of proper physiological utilization of the vitamins, is still in the process of investigation. In a previous article[8] it was demonstrated that a comparatively high percentage of normal aged individuals showed evidence of hepatic impairment, as determined by at least one or more of five separate liver function tests. In another study it was shown that vitamin A was not synthesized at a normal rate from the available dietary carotene.[5] This may also point to hepatic dysfunction, although this point is still a debatable one.[9] There is still another possibility which may be offered as explanation for "biochemical avitaminosis" in the aged, namely, that these

phenomena are mainly physiological, and that the standards which are usually applied to children and young adults do not hold for elderly individuals.

Another factor which must be taken into account in discussing vitamin utilization in the aged is the diet to which old people become accustomed. It is possible that their diet is so constituted that excessive demand is made upon those vitamins which are ingested with the food, and hence are insufficient in amount although they are adequate for the young adults or children. In an effort to ascertain this fact, an investigation into the dietary habits of a group of 65 normal aged individuals between the ages of 67 and 89 years was undertaken.[6] The average daily protein intake ranged from 66.0 to 97.4 gms. with an average of 83.4 gms., the fat intake varied between 44.8 gms. and 68.3 gms., with a mean value of 58.9 gms. per diem. The daily carbohydrate intake ranged from 203.2 to 286.4 gms., averaging 244.7 gms. per diem. The total daily caloric intake was between 1604 and 2260 calories, with a mean value of 1843 calories. It can be readily seen that the carbohydrates comprise about 52 per cent of the daily diet, in terms of the total caloric intake.

It is possible that elderly people are partial to carbohydrates because of lack of teeth, or perhaps less effort is required to chew this type of food. Another known clinical fact is that in aged individuals a high carbohydrate diet is more easily tolerated. In regard to vitamin B_1, it is generally recognized that the thiamin requirement is influenced by several factors, among which are the nature of the diet and the quantity of food consumed. It is increased by a diet high in carbohydrates.[10]

It was also thought of interest to make a clinical study of some of the persons under investigation to see if any clinical evidence of avitaminosis could be found. Twenty apparently normal aged subjects who ate the usual diet served in the institution were chosen at random and examined carefully for clinical evidence of deficiency.* The criteria for clinical avitaminosis were signs of deficiency on the tongue, the eyes, the lips, especially the angles, the naso labial folds and the skin of the upper arm and the outer aspect of the thigh.

Of the 20 subjects examined, one, a 76 year old male, showed slight fissuring of the angles of the lips, which, however, could have been caused by ill-fitting dental plates which the subject was wearing at the time of examination. However, since the majority of the subjects were edentulous, and wore dental plates without showing the same type of fissuring, it was assumed that this was a sign of vitamin deficiency. In this individual the tongue was slightly magenta, with marked decrease in the number of papillae; there was a slight keratosis of the skin of the upper arm. Another subject, a 74 year old female, had a slight pterygium in one eye and a slight degree of keratosis on the skin of the thigh. None of the other 18 individuals showed any clinical evidence of vitamin deficiency.

Discussion

It can readily be seen from a study of the subject of vitamin utilization in the aged, that the vitamin requirements of normal elderly people cannot be measured in terms of standards applicable to young adults or children. The problem in elderly people is either a physiological one or one of faulty utilization. Irrespective of the cause, the diets of old people must be supplemented by vitamin therapy. While it is difficult to describe the exact amounts necessary in each individual case, it can be safely stated that comparatively large amounts of vitamin supplement should be prescribed. Our clinical experience has shown that at times it is essential to give these vitamins parenterally at the outset and then follow with vitamin therapy by mouth.

The fact that elderly people have "biochemical avitaminosis" based on laboratory data alone, does not lessen the necessity for these vitamins even though the need may be physiological. Further investigations are essential to explain these various phenomena.

*The clinical examinations were made by Dr. Norman Jolliffe.

Summary and Conclusions

1. A state of "biochemical avitaminosis" has been found to exist in the majority of normal aged individuals.

2. The possible causes for the laboratory evidence of avitaminosis have been discussed.

3. The diet in elderly people and its relation to vitamin utilization has been outlined.

4. The need for vitamin supplements in the aged has been stressed.

Bibliography

1. Rafsky, H. A., and Newman, B.: Vitamin B_1 Studies in the Aged, Gastroenterology, 1, 737 (1943).
2. ———, Vitamin C Studies in the Aged, Am. J. Med. Sci., 201, 749 (1941).
3. ———, Porphyrinuria in the Aged, Am. J. Dig. Dis., 9, 43 (1942).
4. ———, Relationship of Niacin to Porphyrinuria in the Aged, Am. J. Med. Sci., 205, 209 (1943).
5. ———, and Jolliffe, N., Carotene and Vitamin A Levels in the Aged, in Press.
6. ———, A Study of the Diet in the Normal Aged Individual, in Press.
7. ———, Vitamin A Tolerance in the Aged, in Press.
8. ———, Liver Function Tests in the Aged. Am. J. Dig Dis., 10, 66 (1943).
9. J. Amer. Med. Assoc., Editorial, 132, 287 (1946).
10. Evans, E. A.: The Biological Action of the Vitamins. University of Chicago Press, Chicago, Ill. (1942), p. 37.

FOURTH ANNUAL MEETING OF THE AMERICAN GERIATRICS SOCIETY

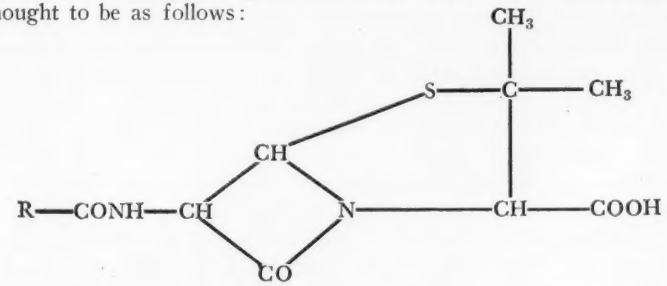
The Fourth Annual Meeting of the American Geriatrics Society will be held at The Brighton, Atlantic City, New Jersey, June 5, 6, 7, 1947.

For further information write to Dr. Malford W. Thewlis, Secretary, 25 Mechanic Street, Wakefield, Rhode Island.

CUTANEOUS HYPERSENSITIVITY REACTIONS TO PENICILLIN IN THE AGED

Joseph Farrington, M.D.

PENICILLIN is a complex organic acid whose structural formula at present is thought to be as follows:



The R-radicle varies depending on the fraction of penicillin analyzed. A recent discovery that penicillin is not a simple compound but a mixture of an unknown number of closely related or similar compounds has had a far-reaching effect on its commercial production and its therapeutic use.[1] Because of its low toxicity, penicillin has been considered an ideal therapeutic agent for the treatment of patients of advanced years. Up to the present time, the reports citing allergic responses have been concerned chiefly with patients in the younger age groups. The skin of elderly people is usually considered to be relatively inactive and the demonstration of intense positive reactions to allergens of any type is unexpected.

References in the literature to allergic phenomena in the elderly are few. Feinberg[2] has written that "an atrophic skin, a skin with poor circulation or skin of the aged may be so diminished in reactivity that what would be ordinarily a moderate reaction may be negative." Tuft[3] has stated that "especially in older individuals or in those who have had their condition for some time, the skin is likely to be of the unreactive type." Wiseman and McCarthy-Brough[4], however, recently reported the death of a 78 year old woman following intradermal testing to dust. In a previous report[5] we have shown that severe reactions, even the dreaded dermatitis

From the Department of Dermatology and Syphilology, College of Medicine, University of Cincinnati, and the Hamilton County Chronic Disease Hospital, Cincinnati, Ohio.

JOSEPH FARRINGTON, M.D., Department of Dermatology, Duke University, Durham, North Carolina, is a graduate of the University of Cincinnati, 1939, B.Sc., B.M., and M.D. degrees. During the war he was Major, M.C., A.U.S., and Chief of Dermatology and Syphilology Section, 234th General Hospital, India.

*THESE studies made possible under a grant from the Bristol Laboratories, Inc., and the Schenley Laboratories, Inc. Crystalline fractions supplied by the Bristol Laboratories, Inc.

exfoliativa, may occur in the aged during the course of penicillin therapy and the cutaneous tests may be positive. The source and mechanism of penicillin allergy in any age group has not as yet been determined. It has been presumed to arise from the Penicillium notatum, from the media, from the chemicals used in the preparation of penicillin, possibly from some intermediary products, or from penicillin per se. Concentrated attempts are now being made in many quarters to localize the source of this allergen. Undoubtedly more than one antigen is involved and for this reason the types of cutaneous penicillin reactions encountered, either in therapy or testing, do not lend themselves readily to classification. It is the consensus of opinion that the clinical features are more important than the cutaneous tests in establishing a diagnosis of penicillin dermatitis. It is now known that there is an allergen common to many fungi and reactivation of other latent fungus infections have been reported during penicillin therapy[6]. Lewis and Hopper[7], in a survey of over 300 patients in a home for the aged, found evidence of residual fungus infections in the skin or nails of over 90 per cent. Gottschalk[8] and her co-workers have been able to produce epidermal sensitivity by repeated application of patch tests with penicillin ointment; we have obtained similar reactions in studies of topical application of penicillin ointment in the aged. If it is a true concept that the aged are not prone to sensitivity reactions, then it would seem advisable to emphasize the ability of penicillin to produce various types of dermatitis in the elderly. The same meticulous care is required in treatment or testing of patients in the geriatric group as in any other. This is exemplified by the following case reports and studies:

Case 1—Serum sickness-like reaction. B.K., a 78 year old white female, developed an acute keratitis caused by a hemolytic streptococcus found on pure culture. She was treated by the intramuscular injection of 50,000 units of penicillin every three hours for five days and made a complete recovery from her eye condition. Twelve days after receiving penicillin therapy there was a sudden onset of a serum sickness-like reaction manifested by fever of 101°F., generalized urticaria, as well as angioneurotic edema of the eyelids, hands and feet. The wrist and ankle joints were swollen. This reaction persisted for ten days despite intensive treatment.

Case 2—Stomatitis venenata due to penicillin. C.P., a 75 year old white male, when first seen was complaining of a sore ear, headache, and generalized malaise. Physical examination revealed a brawny, dark red, indurated, shiny patch of acute dermatitis with well defined edges, involving all of the left external ear and preauricular region of the face. His temperature was 100°F. A diagnosis of erysipelas was made. He was treated with 100,000 units of penicillin orally every three hours, using in succession two commercial brands of tablets. Adequate blood levels were maintained. By the third day of treatment his temperature was normal and most of the erysipelas had faded out. On the fifth day of therapy he complained

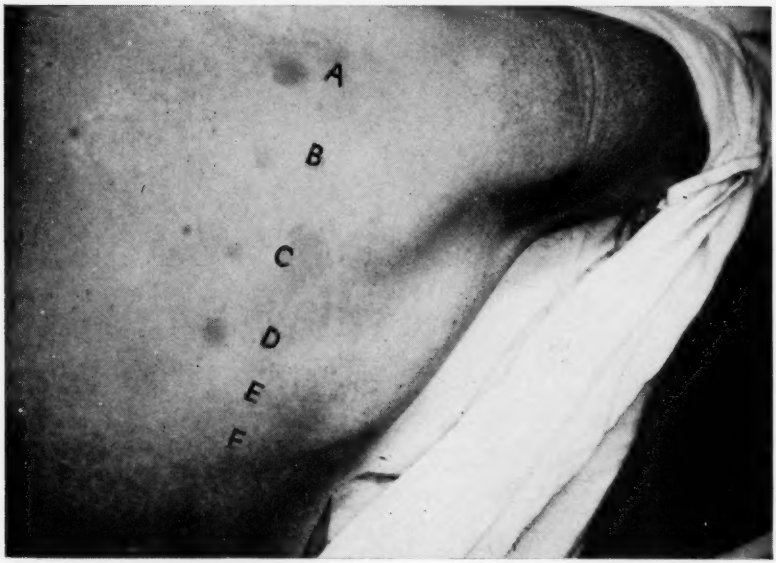


Fig. 1. Cutaneous tests on the back of a 78 year old man. A—the reaction at the end of 72 hours following the intradermal injection of 0.1 cc. of normal saline solution containing 200 units of crystalline sodium penicillin K. B— and C—show reactions at the site of subcutaneous injections of 150 and 100 units of penicillin K. D—shows the reaction following the intradermal injection of only 2.5 units of crystalline sodium penicillin K. Smaller amounts of penicillin injected intradermally at E— and F— provoked no cutaneous response.

of pain and tenderness of the tongue and throat. Examination revealed the buccal mucosa, tongue and anterior pharynx to be fiery red, moderately edematous and tender but no vesicles were seen. He was thought to have a penicillin stomatitis venenata and the ingestion of tablets was discontinued. The inflammatory reaction in the mouth receded in forty-eight hours. One week later contact testing of the buccal mucosa showed a positive reaction after one hour contact time with the commercial tablets used. Control studies with all the ingredients of the tablets except penicillin were negative.

After observing these and additional cases showing other types of penicillin dermatitis, 111 elderly patients, all of whom were over sixty-five years of age, were included in a larger group of patients subjected to the experimental topical application of a penicillin ointment containing 500 units per gram. The test sites included the left forehead, left cheek, left neck and all surfaces of the left forearm midway between the elbow and wrist. Four patients, or 3.6 per cent, developed dermatitis of the face. Two were elderly men, aged sixty-five and eighty years respectively, who exhibited a contact type of eczematoid dermatitis over the face in seven days; two women, aged seventy-two and the other seventy years, developed a similar

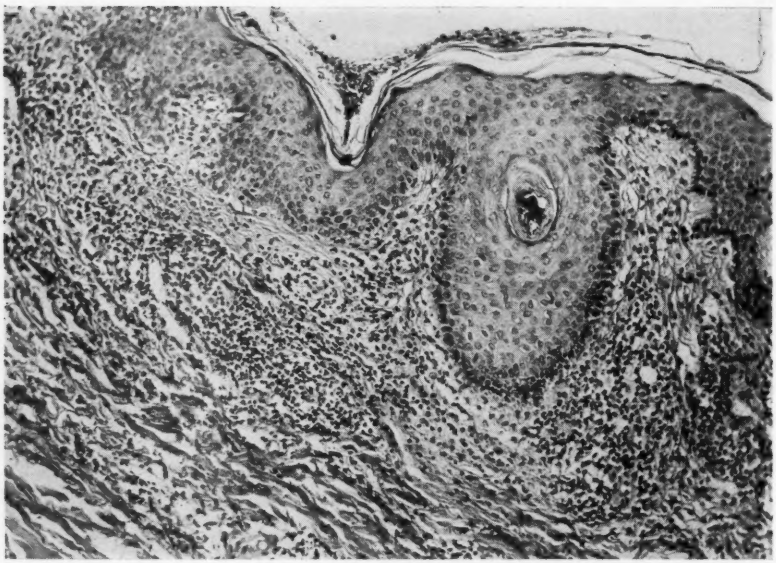


Fig. 2. Photomicrograph of a microscopic section from test site A— shown in Fig. 1. Note the lymphocytic infiltrate, areas of spongiosis, slight acanthosis and extensive edema of the pars papillaris. There is also some fragmentation and separation of the collagen fibers.

type of dermatitis in five days. No penicillin reaction was noted over the other areas of the body. It has not as yet been determined why penicillin contact dermatitis apparently develops more easily on the face.

Of the patients showing positive sensitivity reactions to penicillin, one had chronic psoriasis and a polyvalent sensitivity to coal tar and many of its derivatives. Contact mucous membrane tests on this patient after the method of Goldman and Goldman[9] showed a positive sensitivity reaction to penicillin. We have previously reported studies of contact testing of the buccal mucosa with special reference to penicillin[10, 11]. We have also shown that in elderly patients who exhibit hypersensitivity reactions to penicillin therapy these reactions may be correlated with positive intradermal (Fig. 1) and patch tests.[5] Biopsy studies of these tests substantiate the fact that elderly people may react vigorously to the intradermal injection of penicillin (Fig. 2) as seen by the character and degree of the cellular infiltrate.

Conclusions

Cutaneous hypersensitivity reactions to penicillin may occur in the aged and furnish additional proof that penicillin is a good sensitizing agent.

The writer is indebted to Paul Seebohm, M.D., and to Alfred Flarsheim, M.D., of the resident staff of the Cincinnati General Hospital and of the Hamilton County Chronic Disease Hospital, respectively, for technical assistance.

REFERENCES

1. Poole, E.: Recent Developments in Penicillin Therapy, MD 1:7 (July), 1946
2. Feinberg, S.: Allergy in Practice, Chicago, 1944, Year Book Publishers, Inc.
3. Tuft, L.: Clinical Allergy, Philadelphia, 1937, W. B. Saunders Company.
4. Wiseman, J., and McCarthy-Brough, M.: Skin Sensitivity in the Aged—Fatality Following Intradermal Tests, J. Allergy, 16:5 (Sept.), 1945.
5. Farrington, J., and Tamura, J.: Cutaneous Testing in a Case of Exfoliative Dermatitis Caused by Penicillin, Arch. Dermat. & Syph. (in press).
6. Schnurman, A.: Latent Trichophyton Infection Activated by Penicillin, Va. Medical Monthly, 72:28 (June), 1946.
7. Lewis, G., and Hopper, M.: An Introduction to Medical Mycology, Chicago, 1943, Year Book Publishers, Inc.
8. Gottschalk, H., and Weiss, R.: Epidermal Sensitivity to Penicillin, Arch. Dermat. & Syph., 53:4 (April), 1946.
9. Goldman, L., and Goldman, B.: Contact Testing of Buccal Mucous Membrane for Stomatitis Venenata, Arch. Dermat. & Syph., 50:79-84 (Aug.), 1944.
10. Goldman, L., and Farrington, J.: Contact Testing of the Buccal Mucous Membrane with Special Reference to Penicillin. Annals of Allergy, 4:6 (Nov.-Dec.), 1946.
11. Farrington, J.: Modifications of the Goldman Technique for Contact Testing of the Buccal Mucosa. J. Investig. Dermat. (in press).

CONFERENCE ON "HEALTH IN AN AGING POPULATION"

A conference on "Health in an Aging Population" was held on March 13, 1947, at the Rochester Academy of Medicine, New York. It was sponsored by: The Council of Rochester Regional Hospitals; Council of Social Agencies; Medical Society of the County of Monroe; New York State Department of Health; Rochester Academy of Medicine; Rochester Board of Education; Rochester Health Bureau; Tuberculosis and Health Association of Rochester and Monroe County, Inc.; University of Rochester, School of Medicine and Dentistry; Visiting Nurse Association.

Speakers at the morning session were: Dr. Edward Stieglitz, Internist and Chief of Staff, Suburban Hospital, Bethesda, Maryland, "The Effect of Aging on the Individual" and Prof. Earl Koos of the University of Rochester, New York, "The Effect of Aging on Society."

A symposium on "Diseases of Advancing Years" consisted of scientific addresses by speakers representing the various branches of medicine:

(1) Internal Medicine
Dr. William McCann-University of Rochester School of Medicine and Dentistry.

(2) Surgery
Dr. Samuel Stabins-Chief of Surgery, Genesee Hospital.

(3) Psychiatry
Dr. Kenneth Slaght-Rochester State Hospital.

(4) Public Health and Preventive Medicine
Dr. Charles M. Carpenter-University of Rochester School of Medicine.

The afternoon session featured a panel discussion on "Environmental Problems of the Aging." Subjects were: Nutrition, Employment, Housing, Recreation, Nursing Care, Training Youth to Assist with Problems of Old Age, and Community Resources for the Aged.

At the evening session, an address by Dr. Louis Dublin of the Metropolitan Life Insurance Company concluded the meeting.

It is hoped that this conference will serve as a pilot demonstration for conferences on the aged on a national scale.

PHYSICAL FITNESS AND WORK CAPACITY OF OLDER MEN

Ernst Simonson, M.D.

THE employment of older people is an important problem in the present and will become more so in the future, due to the continuous age shift of the population. It is estimated that within 40 years about 40 per cent of the total population of the United States will be over 45 years of age[1], which is similar to the trend in other countries. If employment of older people does not more or less parallel the age shift, serious socio-economic consequences will result. This leads to the fundamental question: is increase of life expectancy associated with a better maintenance of working capacity? It is known that the work capacity in an individual decreases with age, but the present problem is an attempt to determine whether the increased life expectancy is associated with a general increased ability to work in the older age groups. If this is the case, an extension of the period of employment is feasible without any great change in work. If, however, extension of the life expectancy is not paralleled by a similar age extension of working capacity, industrial jobs must be adapted to the working capacity of older men in order to maintain their employment. This would be a formidable, but by no means hopeless, task.

The second important question is: Do the various physiological, biochemical and psychological functions deteriorate with age at the same rate? It is known that various physiological functions change at a different rate with age, several quite rapidly, while others are age-resistant to a high degree. To meet present and future demands of industry, it would be necessary to analyse jobs as to the degree of involvement of age-resistant functions in various types of industrial work. On the basis of such material, older workers could be assigned to jobs they would be able to do at a high degree of efficiency. Such redistribution of older workers is now being attempted to some extent, but in a rather arbitrary way. It is also important to know whether there are any special factors which might affect the drop in working capacity of an individual with age.

This leads us to the third fundamental problem: Is it possible to counteract or to delay the decrease in working capacity with age? It might be objected that the probability of counteracting a natural process is slight. Some evidence is available, however, which seems to indicate that if not the process of aging, at least its rapidity can be influenced to a certain de-

From the Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis, Minn.

ERNST SIMONSON, M.D., is Associate Professor of Physiological Hygiene and Physiology, University of Minnesota, and a member of the Committee on the Nutrition of Industrial Workers, National Research Council; American Physiological Society, Society for Experimental Biology and Medicine; American Association of University Professors.

gree. It is possible, for instance, that the process of aging is accelerated by unfavorable living and environmental conditions in a large part of the population. If this is the case, improvement of these conditions may slow down the speed of aging. Before discussing the information available on these three fundamental problems, it is well to emphasize its scarcity. Much further work is needed for any definite conclusions, but some of the results obtained so far are intriguing.

Parallelism Between Life Expectancy and Maintenance of Work Capacity

In order to contribute to this fundamental question, investigations must be performed over a long period of time. Only a few decades ago when such work should have been started there was no reason to expect the increase of life expectancy that has occurred in all civilized countries. In other words there appeared to be no reason to initiate such investigations. This explains the absence of systematic studies in this direction. Even now with our knowledge of the mortality trends which are likely to continue, few, if any, authors are ready to begin a comprehensive study of work capacity in a large sample of the population, in the hope that such investigations can be repeated in 20 or 50 years. And yet, such long range studies are extremely important. Therefore, it is a lucky accident that two entirely independent investigations, neither undertaken with such purpose in mind, can be used to throw some light on this question. Both series concern the decline of muscle strength with age, a function with a very marked age trend and, at the same time, important for the overall working capacity.

In 1836, Quetelet[2] investigated muscle strength in different muscle groups on a rather extensive scale in Belgium by means of spring coil dynamometers. The maximum back muscle strength was attained as a short peak at the age of 27 years, after which it dropped rather rapidly, so that at the age of 30 to 35 years it was only 94 per cent of the peak strength, at the age of 40 to 45 it was 89 per cent, and at the age of 50 years only 82 per cent.

Eighty-five years later, in 1921, Rejs[3] investigated muscle strength in a group of 3,000 Dutch men and women. Holland and Belgium are geographically so close that both series are comparable, so far as population, climatic or living conditions are concerned. The population in both countries is reasonably stable, so that the type of population probably did not change essentially during that interval. In Rejs' series, the maximum strength was maintained at a level for several years until the age of 37; at the age of 40 to 45 years it was still 96 per cent of the maximum and at the age of 50 still 92 per cent. The decline of muscle strength at the age of 37 years in 1836 was about the same as that at the age of 50 years in 1921. In the same period, the life expectation for males in Holland in-

creased from 34.9 years to 55.1 years, according to Dublin and Lotka[4]. No data for Belgium are available for the whole period, but for the periods 1881-1890 and 1891-1900, the life expectation in Belgium was very close to that in Holland. However, in the later periods (from 1920), according to a personal communication from Dr. Dublin, the life expectancy became definitely better in Holland than in Belgium, the difference amounting to 7.8 years for 1930. It is, of course, possible that the 1921 data of the muscle strength might have been somewhat different in Belgium. However, the over-all trend is unquestionable, and the comparison of Quetelet's with Rejs' results seems to imply that the increased life duration is associated with a better maintenance of muscle strength, and possibly also of other functions important for the over-all working capacity.

It should be emphasized, however, that the parallelism in the life expectancy and maintenance of muscle strength does not necessarily prove a causal relationship. There are many accidental factors such as motivation, occupation, state of muscular training, differences in body build which might possibly account for such differences and which have not been eliminated in Quetelet's and Rejs' material. However, their results are at least suggestive to a certain degree. In case that there is a definite relationship between life expectancy and maintenance of muscle strength, it might be assumed, although without any direct proof, that the same factors which account for the improvement of life expectancy might also account for the better maintenance of muscle strength, and it is quite likely that the rising living standard is responsible for both. There was a rather steady and remarkable increase of the standard of living in Western and Central Europe during the past 90 years. The relationship between living standard and mortality rate is well established.

There is also some indirect experimental evidence available to show the influence of the standard of living on muscle strength. Vernon[5] compared the muscle strength of 10.593 employed men with 1,328 unemployed men. The average strength of the lumbar pull of the employed men was 362.6 lb., that of the unemployed was only 313.9 lb. A group of 1,735 students had an average strength of 366.5 lb. These differences parallel in a general way the differences in the standard of living of these groups, although, of course, the standard of living cannot be defined in a simple mathematical way.

That a better maintenance of muscle strength with age, with increasing life expectancy, has importance for the prolongation of employability can be implied from Ascher's[6] studies. Ascher found that in industrial jobs which require muscular exertion, the average wage earning power declines parallel to the decline of muscle strength. There was, in a large railway repair shop, an outspoken parallelism between the decrease of earning power with age and the involvement of muscular effort in different jobs. In jobs with heavy muscular exertion the decrease of earning power paral-

leled the decrease of muscle strength in Rejs' curves. Obviously, younger workers will always be preferable for heavy exertion, but the age scale has probably improved during the past decades.

MATCHING OF INDUSTRIAL JOBS TO THE CAPACITY OF OLDER WORKERS

For a proper matching of jobs and older workers it is necessary to know the rate with which various functions decline with age and the degree of involvement of such functions in various jobs.

From the point of employability it would be important to know whether the drop of muscle strength is uniform in all muscle groups, or whether this process occurs in various muscle groups at a different rate. Rejs'[3] data show that the strength of the back muscles drops faster with age than the strength of arm and hand muscles. This has been corroborated by Ufland[7] in Russia. According to his findings, the strength of the back muscles reverts to their value at the age of 20 years between 30 and 39 years. This is faster than in Rejs' subjects; the difference might well be explained by the difference in population and the higher standard of living in Holland. The same drop occurs in the biceps between 40 and 49 years and in handgrip strength between 50 and 59 years. Handgrip strength appears to be much better maintained with age. It is questionable whether the different rate of decline reflects true physiological differences of muscle strength; the willingness to exert themselves might be greater for localized effort (handgrip) in older men. Whatever the reason for the different rate of decline in various muscle groups might be, the data are practically important; they suggest that comparatively little interference of age with tasks involving only hand muscle strength can be expected, while on the other hand, prolonged standing or even unsupported sitting seems to be a greater strain for older workers. Therefore, introduction of suitable back supports is advisable for older workers.

Muscle strength is, of course, not the only muscular function which declines with age. In fact, the decrease of the maximum working capacity for hard work with age is more pronounced than the decline of muscle strength. This is due to two factors: the ability of lactic acid formation or accumulation declines from 40 years[8] and the maximum oxygen intake declines from 20 years of age. According to Robinson, the maximum O_2 intake per kilo. of body weight is 52 cc. at the age of 20 years, 45 cc. at the age of 30 years, 41 cc. at 40 years, 38 cc. at 50 years, and 35 cc. at 60 years. The decline of the lactic acid formation interferes with the ability to do anaerobic work, i. e. work of such intensity that no adequate oxygen supply is possible. Again, it is questionable whether the differences in lactic acid formation reflect a true physiological difference between older and younger men; it is also possible that the lower levels of lactic acid in older men result from the inability or unwillingness to exert themselves to the same degree as younger men do. The decline of the maximum oxygen intake characterizes the decline of the maximum level of energy available for

a more sustained effort. On the other hand, older men can perform moderate work at the same mechanical efficiency as younger men can. Although maximum muscular effort is very rarely required in industrial jobs, the findings are important nevertheless. They show that older men, even when working at moderately heavy exertion, are much closer to their limit than younger workers would be; in other words, they have a much smaller reserve left. There is reason to believe that the onset of fatigue is related to the reserve capacity; a rate of work close to the limit of the maximum oxygen intake is apt to produce fatigue faster than a rate of work far below that level would be. For this reason, even a type of work involving only moderately heavy muscular effort would be more fatiguing for older men. On the other hand, Robinson's value of 35 cc. of maximum oxygen intake per kilo at the age of 60 years would correspond to 2100 cc. for a man of 60 kilos body weight. There are many younger normal men whose maximum oxygen intake is far below this level[9]. Therefore, considerable overlapping of the various age groups in regard to maximum work capacity as expressed by the maximum oxygen intake should be expected, although, as a whole, there is a group inferiority of older men to do heavy or moderately heavy muscular work.

The lower maximum oxygen intake in older men is associated with a lower pulse rate. Dill[10] concluded that the inability of older men to increase the pulse rate to the same extent as younger men is the limiting factor for the maximum oxygen intake. Robinson's findings that the increase of the oxygen intake during work proceeds slower in older men, probably due to a slower circulatory adjustment, seem to support this view. On the other hand, clinical evidence speaks against this assumption. The rate and distribution frequency of tachycardia even in pathological conditions is not materially affected by age. Important as circulatory functions are, one should not overlook the fact that fatigue in man is generally a central nervous system phenomenon; fatigue indicates the tolerance of the central nervous system against changes in the composition of tissues or fluids produced by exercise. It seems more likely that the maximum oxygen intake and the pulse rate were lower in older men because they felt fatigued at a lower level of performance. This view is supported by unpublished experiments performed by the author together with N. Enzer and R. Benton. The performance in several types of work of a group of 25 younger men (average age 33.3 years) was compared with that of a group of 11 older men (average age 53 years). Both groups were selected from a large number of volunteering employees of the Northwestern Mutual Life Insurance Company, whose co-operation was excellent. Both groups were requested to run at maximum speed until exhaustion. The speed, total time, and especially the distance run by the older men were much lower. The distance covered until exhaustion by the older men was about half that of the younger men, and there was practically no overlapping. The

increase of the pulse rate of the older men was less than that of the younger men, in agreement with Robinson's and Dill's findings. On the other hand, the depression of the fusion frequency of flicker (f.f.f.) immediately after the run was more pronounced in the older men. There is ample evidence to show[11-14] that the f.f.f. indicates the excitability of the retin-cortical system and probably is related to that of the whole central nervous system. The decrease of the f.f.f. after the run is probably due to the inadequacy of oxygen suply (oxygen debt) produced by the excercise[15]. Since lighter exercise produced the same or even a greater decrease of the f.f.f. in the older men than harder exercise did in younger men, it would appear that the decreased endurance for maximum work of older men is due to a large degree to a decreased tolerance of the central nervous system probably to oxygen want. The lesser increase of pulse rate is obviously secondary and due to the smaller amount of work performed until fatigue. In two types of standardized sub-maximum work (genuflexions, pulley exercise) the increase of pulse rate was about the same in both age groups.

In contrast to the decrease of maximum work endurance, the endurance for static work (holding an 8 pound dumbbell horizontally with outstretched arms) was not decreased in older men, in fact, the average value was slightly better, although the difference was statistically not significant. This finding is rather important in view of the widespread occurrence of static work or static components in industrial jobs.

The capacity of older men to do work requiring only light muscular effort depends on the maintenance of manual skill with age and on the maintenance of visual performance. Visual control is of much greater importance for types of light muscular work such as assembly work or office jobs, than it is for types involving muscular exertion.

Loss of the range of accommodation and changes of the refraction of the eye with age are very well known, so that older persons have to use extra lens power to see clearly at close distances. Tiffin's[16] investigations on 7,000 steel mill workers have shown that glasses, either for general use or for close vision only, are more common among employees rated high in labour efficiency than among those rated low. The discrepancy increases sharply after the age of 50. In younger people, those wearing spectacles have a lower average acuity than those who do not use spectacles. Therefore the curves of the drop of acuity with age for people wearing glasses and for those without glasses cross at the age of 50 years. Before 50 years of age acuity is better in the group without glasses while after this age it is better in those wearing glasses. Among those older people wearing glasses after prescription, 77 per cent passed the near acuity test. Among those who carried "reading glasses" (mostly bought without adequate professional services), only 25 per cent passed the test. This shows that professional eye care, not simply the purchase of spectacles, is essential to maintain or improve industrial performance in older people.

Tiffin also demonstrated in a large number of cases the influence of age on colour (red-green) discrimination. Between the age of 20 to 30 years, about 73 per cent passed a simple test of red-green discrimination. The percentage dropped with age; after 55 years, only 30 per cent were able to pass the test. On the other hand, stereopsis (depth perception) reaches a maximum level between 40 and 50 years, from which it drops slowly up to the age of 60 (where it equals the age group 20-30) and then falls abruptly. It appears that people between 50 and 60 will not be incapacitated in jobs requiring depth perception (crane operators, workers on elevated structures, carpenters, machinists, filing clerks, etc.).

The size of the maximally dilated pupil diminishes with age, so that they admit only about one-half as much light at the age of 50 as they do at the age of 20, the average diameter decreasing steadily up to the age of 80 years. In addition, the magnitude of pupillary changes with changing brightness diminishes with age, so that older people are deprived of the advantages of pupillary adjustments and are especially handicapped at low levels of illumination.[17] The influence of age and other fundamental functions (light and dark adaptation, perception of movement, perception of contour, resistance to glare, and contrast discrimination) has not been sufficiently explored, while the decrease of the fusion frequency of flicker with age has been safely established.[18-19] Due to the general impairment of vision with age, it seems advisable not to employ older people in jobs with more than average visual requirements or with high incidence of eye strain. On the other hand, the effect of these visual handicaps on visual fatigue of older men has not been actually investigated.

Fine muscle co-ordination and speed of small muscle groups also appear to decline with age, according to results obtained under laboratory conditions by Miles[20] and Smith.[21] The decline of fine assembly performance with age was more pronounced at higher speed. On the other hand, the working capacity of older men, expressed by the average wages, is well maintained in jobs with finer manipulations (Ascher) up to the age of 60 years, in contrast to types of work demanding considerable force of large muscle groups. Stieglitz[1] and Kossoris[22] came to the same conclusion from observations in industry. The discrepancy between laboratory experiments and observations in industrial plants can be explained with the factor of training. Job experience might compensate to a large extent for some physical handicaps. This is substantiated by Miles'[23] observations that in older men who had mechanical training, the manual dexterity, determined by means of the Link McFarland Cube Assembly test, was maintained into late maturity, in contrast to the gradual decline with age in the general population. It seems, therefore, that the increasing of sickness and accident absenteeism are important. The discussion was of sickness and accident absenteeism are important. A rather large material replacement of muscle power by machine power, which is a parallel, although

independent, development of the increasing age shift of the population, facilitates the employment of older men.

Possibility of Counteracting the Process of Aging

Information on this problem is practically non-existent but some general suggestions are possible. The better maintenance of muscle strength which seems to have occurred during the past 6 or 8 decades is probably due in general to the improvement of the general living standard, as discussed formerly in this article. It would appear, then, that a general further improvement might delay the process of aging. The effect of diet is of great importance in delaying the effects of age as shown in animal experiments,[24] although no generalization of these results to humans is possible.

Schochrin[25] found that in a large group of workers with predominant activity of one arm (right or left) the drop of muscle strength with age was more pronounced in this particular limb, usually the right arm and hand muscles. It seems that activity restricted to a few muscle groups could accelerate the natural process of decline of muscle strength with age in these muscles, so that distribution of the work to several muscle groups might better maintain working performance with age.

It is interesting to investigate how far the reduction of sex hormone production with age might be responsible for the reduction of muscle strength and endurance. If the reduction of sex hormone were partially responsible for the drop of working capacity, it might be expected that administration of sex hormone would improve the performance.

In a recent series of experiments[26] 6 men from 51 to 68 years were treated with methyltestosterone for a period of from 6 weeks to 10 months in a dosage of 30 to 40 mg. a day. This group was somewhat preselected; all subjects complained of fatigue or loss of working capacity, but no clinical symptoms of any disease could be found. Complaints of fatigue after 45 to 50 years are very common when the loss of working capacity with age becomes more or less noticeable. In this respect, the experimental group was probably typical of a rather large part of the population. The effect of methyltestosterone treatment was controlled by placebos given for a period of from 4 to 6 weeks. After methyltestosterone treatment, the fusion frequency of flicker was increased from 4.2 to 12 flashes, on the average by 7 flashes. In 4 of the subjects the pre-treatment fusion frequency was slightly subnormal, indicating a substandard condition of the central nervous system. In these subjects, after methyltestosterone treatment, the values were well within normal limits.

The endurance in weight lifting (dynamic work), performed at constant load and rate, increased in four subjects from 36 to 290 per cent; no increase was noted in the fifth subject and in the sixth this type of work could not be investigated.

Endurance in static work (holding a load) increased between 27.0 and 41.5 per cent in four subjects, about 100 per cent in the fifth subject, while no measurement could be made in the sixth subject. The strength of the back muscles increased from 26.8 to 68.2 per cent, (on the average of 43.5 per cent). No increase of the strength of arm extensors was noted, while four subjects showed also an increase of the handgrip strength which occurred later and to a lesser degree than the increase of back muscle strength.

The prominent action of methyltestosterone treatment on the back muscles is interesting because the drop of strength with age is more pronounced in this muscle group than in any other. This may be regarded as good corroboration of the view that some effects of aging are due to the drop of sex hormone production, so that administration of male sex hormone might counteract these effects. This conclusion is also supported by Samuels, Henschel and Keys' results[27] who failed to increase muscular performance with methyltestosterone in normal young men, in whom the production of sex hormone is at the maximum level.

It is, of course, questionable as to how far these conclusions may be generalized. Our experimental group was small and somewhat pre-selected in that the symptoms of subjective fatigue were probably over-average. Treatment in older men who do not complain of exaggerated fatigue may be less or not effective. Obviously, these results have more theoretical than practical value. The treatment might delay some secondary effects of sex hormone secretion, but the primary process of the aging of the sex glands is probably not influenced. Nobody would suggest that the working capacity of older men be maintained by prolonged methyltestosterone treatment, especially as the present evidence is too small to warrant such a suggestion.

It appears to be much more practical to find a solution for the employment of older men by a better matching of job and age and in improvement of the general work conditions. It is known, for instance, that the introduction of rest-pauses in industry benefits especially the slower and weaker workers. It is to be expected, therefore, that the systematic introduction of rest-pauses would be still more important for older workers than it has been demonstrated to be for younger workers.

According to the present material available, it would appear that the employability of older men for jobs not demanding heavy muscular effort, prolonged standing, or discrimination of fine details is in general not restricted by physiological handicaps. To a large degree, some physiological inferiority can be compensated by technically minor improvements of working place or work organization. These factors, however, are not the only ones important for employability of older men. The tolerance against heat, humidity, noise, dust or fumes has also to be taken into consideration. Very little information is available yet in this respect although there is some evidence that humidity tolerance decreases with age.[28] For office jobs, age trends of intellectual performance are fundamental. Also age trends

restricted to older men because no investigations have been performed regarding older women, and as yet, even the material on physical fitness and work capacity of younger women is extremely scanty.

References

1. Stieglitz, E. J.: Aging as Industrial Health Problem. J.A.M.A., 116:1383-87 (1941).
2. Quetelet: Sur l'homme et le dévelopment de ses facultés. Bruxelles (L. Hauman and Cie) (1836).
3. Rejs, J. H. O.: Über die Veränderung der Kraft während der Bewegung. Pflüger's Arch. Physiol., 191:234 (1921).
4. Dublin, L. I., and Lofka, A. J.: Length of Life. New York, Ronald Press Co. (1936).
5. Vernon, H. M.: Health in Relation to Occupation. Oxford Univ. press., London (1939).
6. Ascher, L., and Baumgarten, P.: Beiträge zur Kenntnis der körperlichen Beschaffenheit der arbeitenden Bevölkerung. Veröff, Med. Verwalt, 19:487-549 (1925).
7. Ufland, J. M.: Einfluss des Lebensalters, Geschlechts, der Konstitution und des Berufs auf die Kraft verschiedener Muskelgruppen. Arbeitsphysiol., 6:653-663 1933).
8. Robinson, S.: Experimental Studies of Physical Fitness in Relation to Age. Arbeitsphysiol., 10:251-323 (1938-39).
9. Knipping, H. W.: Ueber die Kontrolle der Herzleistungsgrenze in der Klinik. Dtsch. Med. Wchnschrft., 63:462-464 (1937).
10. Dill, D. B.: Effects of Physical Strain and High Altitudes on Heart and Circulation. Am. Heart J., 23:441-454 (1942).
11. Simonson, E., and Enzer, N.: Measurement of the Fusion Frequency of Flicker as a Test for Fatigue of the Central Nervous System. J. Indust. Hyg. a. Toxic., 23:83-89 (1941).
12. Simonson, E., Enzer, N., and Blankstein, S.: Effect of Amphetamine (Benzedrine) on Fatigue on the Central Nervous System. War Med., 1:690-695 (1941).
13. Enzer, N., and Simonson, E.: The Effect of Small Doses of Alcohol on the Central Nervous System. Am. J. Clin. Pathol., 14:333-341 (1944).
14. Walker, H. E., Woolf, J. I., Halstead, W. C., and Case, I. J.: Mechanism of Temporal Fusion Effect of Photic Stimulation on Electrical Activity of Visual Structures. J. Neurophysiol., 6:213 (1943).
15. Simonson, E., Enzer, N., and Benton, R. W.: The Influence of Muscular Work and Fatigue on the State of the Central Nervous System. J. Labor. a. Clin. Medic., 28:1555-1567 (1943).
16. Tiffin, J.: Industrial Psychology, New York (1942).
17. Luckiesh, M., and Moss, F. K.: The Science of Seeing. Van Nostrand, New York (1937).
18. Simonson, E., and Enzer, N.: The Influence of Age on the Fusion Frequency of Flicker. Journ. Exp. Psychol., 29:252-255 (1941).
19. Brozek, J., and Keys, A.: Changes in Flicker Fusion Frequency with Age. J. Consult. Psychol., 9:87-90 (1945).
20. Miles, W. R.: Performance in Relation to Age. In "Mental Health in Later Maturity." U. S. Public Health Reports. Suppl. No. 168, p. 34-42 (1943).
21. Smith, K. R.: Age and Performance in a Repetitive Manual Task. J. Appl. Psychol., 22:295-306 (1938).
22. Kossoris, M. D.: Relation of Age to Industrial Injuries. Monthly Labor Rev., 51:789-804 (1940).
23. Miles, W. R., and Miles, C. C.: Principal Mental Changes with Normal Ageing. Chapter 5 in Stieglitz' "Geriatric Medicine," p. 99-117, Philadelphia (1943).
24. McCay, C. M.: Chemical Aspects of Ageing. E. V. Cowdry, "Problems of Ageing," Chapter 21, p. 572-623 (1939).
25. Schochrin, N.: Gigiena Truda 1928, No. 5, 29.
26. Simonson, E., Kearns, W. M., and Enzer, N.: Effect of Methyltestosterone Treatment on Muscular Performance and the Central Nervous System of Older Men. Jour. Clin. Endocrin., 4:528-534 (1944).
27. Samuels, L. T., Henschel, A. F., and Keys, A.: Influence of Methyltestosterone on Muscular Work and Creatinine Metabolism in Normal Young Men. Jour. Clin. Endocrin., 2:649-654 (1942).
28. Brinton, P. H., Seifert, H. E., and Frasier, E. S.: Disabling Morbidity Among Employees in the Slaughter and Meat Packing Industry, 1930-34, inclusive. U. S. Pub. Health Repts., 54:2196-2219 (1939).

GERIATRICS

Official Journal of the American Geriatrics Society

OFFICERS OF THE AMERICAN GERIATRICS SOCIETY

WALTER E. VEST, M.D., *President*
EDWARD B. ALLEN, M.D., *First Vice President*
HOLLIS E. CLOW, M.D., *Second Vice President*
MALFORD W. THEWLIS, M.D., *Secretary*
RICHARD J. KRAEMER, M.D., *Treasurer*

Correspondence pertaining to the American Geriatrics Society should be addressed to Dr. Malford W. Thewlis, Secretary, 25 Mechanic Street, Wakefield, Rhode Island.

THE FEAR OF DEATH

NICODEMUS went to Christ in the night in search of everlasting life. Ponce de Leon roamed the New World, seeking the fountain of perpetual youth. Steinach severed the *vas deferens* in an effort to rejuvenate old men and stimulated interest in gland transplants and gland fathers. Life has always been held in precious esteem but when we say that we want to live a long time, do we not have in mind its perfections and forget to count life's disappointments?

Owen Meredith gave us in poetic verse "The Apple of Life." The theme was that whoever ate the apple would be assured of living forever. The author described how several persons in different stations in life reacted to this proposal. The apple was first offered to King Solomon. After careful consideration of the consequences he rejected it but passed it on as a favor to his fair Shulamite. She reached the same decision herself and gave it to her prince. The prince, after due deliberation, did not want it and tendered it to his Egyptian sweetheart, who in turn carried it to King Solomon. Thus, the wisest of all men renounced it twice. Each person, after debating the advantages and disadvantages of the mysterious charm, voted against the responsibility of changing nature's course.

William Cullen Bryant in "Thanatopsis," and Robert Louis Stevenson in "Requiem" show a beautiful resignation toward death. As physicians, we see men who die with a smile—they are said to be brave. We see those who after lingering illnesses welcome the end, while many are wrapped in the kindly mantle of insensibility that deprives them of feeling and fear.

Fear of death is a motivating factor in the calling of the doctor who sometimes prolongs life, sometimes dispels fear, but always comforts the patient and relieves the pain that may be incidental to the ravaging processes of dissolution. He does all this knowing full well that no one can live forever. Let us be reconciled to believe that it should be as it is. After all, it is not a question of how long we live but how well. It is the function of geriatrics to aid in the prolonging of good lives. A. E. H.

PRECLINICAL MEDICINE AND GERIATRICS

MANY physicians are interested in geriatrics and are even specializing in this branch of medicine. In certain instances this is unfortunate since some younger practitioners who see a future in geriatrics may not be equipped to specialize until they have spent a few years in general practice, and some older physicians, in semi-retirement, may think that specializing in geriatrics will enable them to relax.

The soundest approach to geriatrics may prove to be the preclinical one. The preclinical method is an attempt to determine the patient's vulnerability in specific instances and to advise accordingly. If one assumes that the preclinical period begins at 20, one begins to treat patients at this age, thus preventing, whenever possible, diseases which occur in later life. Patients who have been under such supervision should present a better clinical picture in later years than those who have let nature take its course. Physical defects uncovered by the draft prove that the preclinician has work to do.

The preclinical approach would take care of the patient from the ages of 20 to 40; the geriatric period would be from 40 on. Obviously combining prevention and treatment to prolong life is our goal. A physician who is prevention-minded will practice preventive geriatrics even with persons of advanced age, for example, by correcting an ailment at the age of 70 which might cause serious consequences at the age of 75.

The physician acquainted with family weaknesses can do much to help its members ward off future disease. Thus, a person with a family history of diabetes who is overweight should be advised to reduce to normal weight as a precautionary measure. A man with a background of cardio-vascular-renal disease, plus a history of cerebral accidents in the family, might avert complications by avoiding unnecessary strain. Coronary occlusion may sometimes be prevented if the patient slows down and functions within his cardiac means. In some instances, also, gall bladder disease might be prevented by a regulated regimen, insuring normal weight.

If a man becomes prevention-minded he soon applies the principle to everyday life—his family, house, property, and equipment—and it is surprising how many hazards can be eliminated if discovered early. More people will live longer and better once they acquire this mental trait.

M. W. T.

YEARS AS A DISABILITY*

IN THE years when there was no premium upon retirement from the military services by reason of a physical disability and when no such premium was to be foreseen, there was a wide-spread attitude among officers of the Army and Navy of keeping their physical ills to themselves and of making light of those that were necessarily uncovered. There were many officers who wanted to remain in service as long as possible, even those who successfully fought off retirement for physical reasons, and who barely dragged themselves across the wire when the statutory age was reached. Such of these as have not been carried off by their ailments have good reason to be regretful of their scorn of being regarded as less than perfect. On the other hand there have been many officers who reached the age of retirement with no definite physical disability and practically no history of injury or illness while in the service. But each and every one of these officers had the disability of being of an age when he was no longer looked upon as a useful cog in the military machine. This officer might have blurred vision, lessened hearing, full dentures, stiffened muscles, hardening arteries, gnarled joints, shortness of breath and a troublesome prostate, all in moderation, and yet neither he nor his examiner could put a finger upon a positive disablement.

Military authorities appear to think that our officers are permitted to go too far into their physical deterioration before they are separated from the service. The statutory age limit is being reduced. Many of us thought we were as good as ever at the age of sixty-four but we were wrong even if our state of preservation was better than the average.

The concept of the Government tax experts has been that this veteran of sixty-four years is a potential competitor in the civilian employment market, while any officer found to have a retirement disability of any kind or from any source is not such. And this is so despite the fact that the Government is making every effort to make the disabled veteran gainfully employable. No informed person will question that the average young amputee veteran has vastly better employment prospects than has the officer of the statutory retirement age. With the advantages of a retirement for disability clearly apparent as they are at present, the gallant wreck that is pictured above has swallowed his pride and presented himself for a medical judgment more often than formerly. And probably medical boards have quite properly found that the cumulative weight of a near dozen minor ailments was quite as disabling as one more serious condition. From whatever cause the proportion of retirements for disability has increased.

Congressional committees are at work upon coming taxation bills and there is evidence that Congress is somewhat repentant of the generosity it has exercised toward the officer retired for disability. A Senate committee has made a report upon tax laws relating to pensions of Federal civilian employees and incidentally to those relating to retired officers of the military services. The committee suggests the limitation of exemption on

salaries "to that portion which reflects disability in the market for civilian employment." It is left to each of our readers to make what he will out of that statement. It suggests a mighty problem in administration.

It is not the purpose to offer any opinion or argument in regard to what exemptions should be made for retired officer personnel. It is hoped that any cuts in the present exemptions will not be heavy. If the thought behind this discussion has been missed, it is that the taxation experts will see the statutory age as of itself a physical disability and that all retired personnel upon reaching that age will automatically become participants in any benefits accorded to the physically disabled.

Col. James M. Phalen, Ret., U. S. Army

*Reprinted from *The Military Surgeon*, February, 1947.

HYPERCHOLESTEROLEMIA AND ATHEROMATOUS DISEASE IN PREMATURE AGING

ATHEROMATOUS disease, usually localized in the coronary arteries, is the most common, single, basic pathological process found in men who have died suddenly and prematurely. The atheromatous plaque has usually enlarged to the point of occluding the lumen or rupturing the intima and precipitating coronary thrombosis with myocardial infarction. Atheromatosis is too complicated a process to have a single cause, yet hypercholesterolemia seems to be a significant factor even though it is only a sign.

In the younger aged group who show definite evidence of coronary artery disease, the blood cholesterol levels have been frequently found elevated. This is particularly so in those who have had a low basal metabolism. Many clinicians and pathologists have noted these facts and attributed a role of importance to the hypercholesterolemia in the development of atheromatous plaques. Hypercholesterolemia is, of course, merely a symptom of a disturbance in lipid metabolism.

Timothy Leary, W. C. Hueper, and others have done many experimental studies and have been impressed by the apparent relationship between cholesterol and cholesterol esters in the blood and in the tissues. Hueper considers the state of the arterial intima as the most important factor. Leary felt that the cholesterols were taken up by the wandering histiocytes of the reticuloendothelial system and these heavily cholesterolized cells left the liver in the blood. He demonstrated, in experimental studies, the penetration of the intima of small arteries and he thus visualized the possible initiation and development of subintimal atheromatous plaques containing cholesterol and cholesterol esters. Hueper has made a very exhaustive survey of all the experimental and clinical material on the subject of atherosclerosis and after much extensive personal experimental work, he concluded that anoxia or coating of the intima in the secondary arteries, would damage the intima and make it more permeable.

Pressure anoxia of the intima develops, particularly at bifurcations,

probably as a result of pressure strain eddies or turbulence that result in increased permeability of the arterial intima incident to secondary local deficiency in oxygenation and nutrition. Pressure on the vasa vasorum and coating of the orifices with collodsial cholesterol might obstruct the intimal circulation and lead to anoxia and increased permeability of the intima. Blood plasma supercharged with cholesterol and lipids or emulsions of these substances, may directly affect the intimal cells and the histiocytes laden with lipids in the liver may penetrate the intima. The mechanism of deposition is unknown. There may be a tissue chemotaxis factor in localization in the form of metachromatic chondroitin or mucoitin.

The invasion and subsequent addition of more fatty histiocytes or emulsions of cholesterol esters by direct penetration of small increments, lead to the development of subintimal atheromatous plaques. These slowly increase in size and the fatty depositions quite often push up under the intima, usually at the bifurcation or at a sharp angulation of an artery seemingly forming a protective pad, but unfortunately encroaching upon the arterial lumen and stretching the intima. The lipid masses in the subintima exert pressure and may again create further ischemia and thus interfere locally with the nutrition of the layers of the arterial walls and thus render the artery more irritable and prone to spastic contraction. Pathological depositions undergo degenerative changes and further stimulate the invasion of fibrosis and subsequent calcification.

Cholesterol and cholesterol esters are relatively inert and are related to the fat only in a tendency to form esters with organic phosphate salts of the common fatty acids. Lipids are found throughout the body cells, particularly in high concentration in bile, blood, milk, liver, kidney, adipose adrenal tissues, and in the egg yolk. Animals and man may also synthesize cholestrol, however, most of it is exogenous and ingested in animal foods. Most of the cholesterol is conjugated in the liver and excreted in the bile and in the feces. Some is reabsorbed in the duodenum and some of it contributes to the formation of hormones. Some cholesterol is utilized within the reticuloendothelial system and the thyroid gland seemingly exerts a regulatory effect upon utilization and deposition of cholesterol. Cholesterol is seemingly handled with difficulty in the adult animal body. The blood levels fluctuate in younger individuals and seem to become fixed in older patients.

There has been a growing feeling among investigators, clinicians, and pathologists that hypercholesterolemia definitely contributes to atheromatosis. Active clinicians are consulted by an increasing number of patients within the age group between 30 and 40 who have suffered attacks of coronary occlusion and who show hypercholesterolemia. They commonly present evidences of hypothyroidism. The family history may often establish a hereditary tendency toward vascular disease of the general type or atheromatosis. Then, too, so often the patient gives a history of long years

of overindulgence in fatty foods, as eggs, cream, butter, animal fats and rich pastries that are considered desirable by gourmets as well as gourmands.

It is to be remembered that cholesterol containing foods are prepared in nature for young animals. It is quite possible that the ability to metabolize the cholesterol in an individual is much better in infancy and childhood than it is after adolescence and in adult life. The ability has been lost by most men, but may be retained by a few. There is much indirect evidence that hypercholesterolemia present over long years apparently has contributed to the atheromatosis. The inability of the body to handle this may well be influenced by the other unknown factors in the development of atheromatosis.

The age-old quest for the fountain of youth and its miraculous rejuvenating elixir is now being lead by biochemists in the search for decholesterizing or lipid mobilizing substances. Dietary regimes, along with the sharp restriction of animal fat intake, are good prophylactic measures, but usually not enough to control situations in which the abnormal chemical processes have gone on for years. The desired substance is one which would promptly decrease the lipid levels in the blood and thus delay the development of subintimal atheromatous plaques. If the high blood cholesterol levels can be reduced, this may contribute, not only towards halting the increase in size, but also, possibly, towards removing part of the fatty substances from the subintimal pathological deposition of cholesterol and cholesterol esters and some other lipids. This is really more than should be hoped for, since in long-established plaques, degenerative changes, fibrosis and calcification have taken place and probably made the process practically irreversible. Some patients proven to have atheromatous diseases have been shown to have normal blood cholesterol levels. Hypercholesterolemia may be refractory to decholesterizing agents.

In the investigations of the past decade, the facts concerning lipid metabolism, the mobilization and the transportation of neutral fats, cholesterol and cholesterol esters in the body have been clarified. The finding of fatal fatty changes in the livers in chronic diabetic and depancreatized dogs maintained on insulin lead Allan et al to demonstrate prevention and cure of this fatty cirrhosis by feeding fresh whole pancreas. This was accomplished later with dried pancreas by Fisher and then with extracts of pancreas by Dragsted, Chaikoff, Wolfe, and others simultaneously by the use of pancreatic extracts. Lecithins and later choline was found by Best and Huntsman to be effective. Several insulin free decholesterizing extracts of pancreas have been prepared and choline, methionine, and inositol have been used to obtain the hepatic normalization which had been produced by fresh and dried pancreas and lecithins. Choline administration was found by Friedlander and Chaikoff to effect a rise in phospholipids.

Clinically, the clearing of ascites and decrease of liver enlargement in early cases of nutritional fatty cirrhosis of the liver in alcoholics has been

demonstrated following the use of choline by Broun and Muether, Russakoff and Blumberg, Herrmann and Rockwell, and others. Lipocaic (Dragsted), lipolysin (Wolfe), and fraction AR (Chaikoff et al) as well as choline, methionine, and inositol, have been definitely established as lipotropic agents. These substances have been shown by biochemists to be mutually related in fat metabolism. They have been found to contribute to the appearance of choline of choline-like substances in the urine, giving a positive reaction with Kraut's reagent. These substances, unlike choline, acetyl choline or mecholyl produced heart block in atropinized animals. Since this group of choline-like substances found in the pancreas and in proteins have been shown to reduce nutritional fatty livers in alcoholics, it seemed likely that they might reduce the abnormal lipids in blood and other tissues. The action is presumable by mobilization or possibly by changing with the help of unsaturated fatty acid, cholesterol into lecithins and lipid phosphorus.

In order to test this hypothesis, several series of 3 year old hens of high egg producing stock were maintained on the standard laying mash and studied. Hypercholesterolemia and high tissue cholesterol levels had been demonstrated in various control series of 26 of these old hens. In two series the additional feeding of choline chloride in 0.5 gram doses to 26 old hens of the same breed showed fairly regular reduction of cholesterol levels in the blood and in the aorta, heart muscle, and liver. The administration of inositol 0.5 gram doses to another series of 3 year old hens had less, but still some, decholesterolizing effect. The administration of methionine in 0.5 gram doses per day to two other series, a total of 23 two-year old hens, had seemingly the greatest decholesterolizing effect.

In patients with hypercholesterolemia and coronary artery disease, the restriction of animal fats in the diet and the administration of potassium iodide and of thyroid extract have been shown to lower blood cholesterol levels after several months to years. The administration of choline, methionine, and inositol, had produced, in a majority of patients, some reduction of blood cholesterol levels and slight rises in lipid phosphorus after 2 to 6 months of treatment. The basic diet is of considerable importance and, in some refractory cases, the exhibition of other substances is probably necessary to accomplish decholesterization. The enzyme systems responsible for the mobilization and degradation of cholesterol to lecithins are still unknown.

The present concepts of the factors concerned in the development of atheromatosis are incomplete. However, there has opened up at least one and perhaps more new approaches to the prevention, postponement, arrest or, possibly, decrease of the subintimal atheromatosis. Atheromatous plaques in secondary arteries are so often of serious significance. Dietary restrictions of the sterol intake and the use of potassium iodide and thyroid extract judiciously in selected cases seem justified. The early successes of administration of other decholesterizing agents seem to offer another promising method of therapeutic attack of the serious processes of premature aging.

George R. Herrmann, M.D.

Digests FROM CURRENT LITERATURE

Aging of Tissues: The Necessity for Research.

WM. DE B. MACNIDER. *Science,* 104, No. 2705:405-406 (November 1), 1946.

The influence of the age of tissues in modifying, if not in determining, types of disease processes in the animal organism has been recognized for centuries, and yet these observations in general have certainly been treated in a superficial, if not an incidental fashion. The phenomena of tissue resistance, as well as susceptibility, in which the factor of age either influences or, in a large measure determines these states as the individual, as organism, advances through different segments of the life span, have not been assigned the importance which they would appear to deserve. This does not imply that the advent of certain specific diseases and tissue modifications of a degenerative order has not been associated in the minds of investigators with such age segments.

Certain diseases have been shown to be due to viruses which prefer an intracellular order of existence. At a certain age period intracellular material would appear to afford a properly chemically constituted culture medium for these living agencies of disease and, as the aging process develops, it may well be that this living medium so changes in its composition that it becomes less appropriate for the life and multiplication of these bodies. Age as a modification in intracellular chemistry, with or without a change in morphology, may have imparted to such cells and to the tissues which they constitute an element of resistance to invasions by disease-producing entities.

If tissue growths come about from a lack of chemical tissue restraint or the advent of a tissue stimulus other than a living invading organism, it would appear equally important that knowledge of a highly complex, difficult-to-obtain and exact order should be searched for in tissues at various age segments in order to explain modifications in tissue susceptibility or resistance to the development of conditions of malignancy. Such states favorable to virus growths, to a lack of tissue restraint, or to tissue stimulation cannot be ascertained until we possess biochemical and biophysical information of cell life at various periods in the life of the organism as a whole in order to contrast chemically through these data periods of the life span of tissues characterized by relative resistance as susceptibility to changes of a malignant order. At the present time diseases of the heart and blood vessels, especially the latter, take the highest toll of life. Such terminal events, in all likelihood commencing years before the finality of the blood vessel accident or episode, certainly show themselves in a much higher percentage in adult and late adult life.

Basic research of a chemical order in an attempt to learn the nature of those chemical changes, the modifications in blood vessel tissue metabolism, and tissue metabolism in general in which those vessels that are associated with aging share, has certainly lagged in its applied interest. This most important problem will be solved only with the discovery of the biochemical constitution of tissues as they advance from an age period of relative nonsusceptibility to vascular disease into that middle-age segment in which their susceptibility is marked, and at whch time such changes often terminate life. As a result of the rapidly increasing life span of the individual, there will be a mounting number of human beings falling in that

diastolic blood pressure shows little age segment in which vascular disease reaches such a state of development as to express itself either in incapacity or death.

The significance of an understanding of aging resides in the assumption that through such information the shifting, adapting, and nonadapting changes of a chemical order of life are to express themselves in determining those age areas in which tissue degeneration make their appearance, in which tissues exert their influence in the formation of new and abnormal tissue growths, or the advent of certain specific states of disease falling in the group of viruses which require an intracellular environment highly specific in its chemical constitution for their propagation.

The Influence of Age on Blood Pressure. A Study of 5,331 White Male Subjects.

HENRY J. RUSSEK, MAURICE M. RATH, BURTON L. ZOHMAN, and ISIDORE MILLER, *American Heart Journal for the Study of Circulation,* 32, No. 4:468-479 (October), 1946.

Although previous studies of unselected groups have demonstrated a progressive rise in *average* systolic and diastolic blood pressure with advancing years, no convincing proof has been offered that *normal* blood pressure increases physiologically with respect to age. Considerable difference of opinion exists, therefore, as to what constitutes the limit of normal at various periods of life. A statistical analysis of the blood pressure levels of 5,331 white male subjects between the ages of 40 and 95 years is presented.

The variations of blood pressure with age and the inferences drawn therefrom are as follows: *Average* systolic blood pressure increases significantly with age, whereas *average* variation after the sixth decade.

The incidence of "normal" blood pressure (149/95 or less) falls markedly with age, so that less than one-half (45 per cent) of the subjects 60 years old and older belong to this group.

The frequency of systolic hypertension rises sharply with advancing years. Approximately one-third (34.4 per cent) of the subpjects of 60 years of age and over show this type of blood pressure elevation. The incidence of diastolic hypertension increases significantly up to the seventh decade, remaining relatively unchanged thereafter.

Normal systolic blood pressure tends to increase with age. The frequency of upper levels of "normal" (140 to 149 mm.) rises appreciably with advancing years. The assumption that *normal* diastolic blood pressure increases with age, is unfounded. Actually, a progressive decrease occurs with succeeding decades, with the result that there is an increasing frequency of low diastolic levels (below 70 mm.) with advancing years.

The rise in normal systolic pressure and concomitant fall in normal diastolic pressure are primarily the result of progressive diminution in the elasticity of the aorta and its large branches associated with the process of aging (vascular factor).

The same physiologic mechanism is responsible for the increasing occurrence of systolic hypertension which is merely the hemodynamic reflection of vascular aging.

Physiologic changes in the central nervous system leading to vascular hyperreactibility with advancing years similarly exert an important influence upon the blood pressure trends of all groups (neurogenic factor).

Both mechanisms (vascular and neurogenic) are summated in their effect upon systolic blood pressure, while exerting opposing influences upon diastolic blood pressure.

The old maxim "100 plus the age" may actually be a fair index of nor-

mal systolic blood pressure. Although the ceiling for normal diastolic blood pressure has been set at 90 mm. Hg., an even lower level appears applicable after middle age.

Essential hypertension cannot be confined solely in terms of systolic blood pressure. It is the diastolic level alone that determines the existence of this disease.

Bibliography of 25 references.

Winter Ailments of the Old

HUGH BARBER. *The Practitioner,* London, 157, No. 941:357-361 (November), 1946.

Tactile and painful sensibility of the skin are diminished in the elderly; however, they are very sensitive to cold. Therefore, in winter, adjustments must be made to suit senile changes. The forearms, wrists and lower parts of the legs need clothing not formerly required. A warm bed, a hot-water bottle and even night socks may be indicated.

Restlessness in day-time because of restricted activity which winter entails may make some mild sedative necessary at night, and is usually more suitable than an hypnotic.

Chronic bronchitis is more likely to end in broncho-pneumonia in later years than in the active period of life, therefore, a bronchial cold in the aged requires great care. A cough may be associated with clear, frothy expectoration which is the result of early cardiac failure. With chronic bronchitis and "winter cough" senile pulmonary tuberculosis is not uncommon. Treatment resolves itself into guarding against secondary catarrhal infection. In all these cases, not only must there be strict confinement to the house, but day and night atmosphere must be warmed, although ventilated.

Pneumonia is a difficult problem; the most common form of pneumonia in old people is generally something in the nature of an infarct related to vascular disease which shows signs of lobar consolidation. Sulfanilamide therapy may prove disappointing in the elderly. When the problem has been solved, that of keeping up the concentration of penicillin in the system with only two injections in the twenty-four hours, this will be the remedy of choice for pneumonia in old people, whatever be the etiology. No doubt some cases beginning by way of infarct or congestion become infected, and for this reason a non-toxic bacteriostatic remedy is indicated.

The practitioner must remember that an elderly patient may be assuming that the span allotted to him is run and, therefore, needs to be told clearly that his illness is one from which he can recover.

Winter climatic conditions also have considerable influence on the circulatory system, although it is more in the nature of inability of the inelastic arteries or the senile myocardium to react to change in temperature than of actual disease. Angina of effort may come to light because of added strain of cold to the circulation, especially when facing cold wind; so also will myocardial weakness be affected by strong wind.

Influenza is a dangerous disease in old age. It is a good example of the insidious nature of disease later in life because in old age there may be signs of pneumonia associated with influenza without warning symptoms.

Herpes zoster ranks high as a disease which may undermine the strength of an old person for a long time, and the intercostal nerves do by no means "suffer in silence." *Osteoarthritis* may be hard to bear throughout the winter. It is during a condition of this sort that every endeavor should be made to keep the mind of the old patient alert. Light meals and mental interest suited to capacity will help spondilitis deformans more than anything sold by the chemist.

As regards the medical aspect of old age, autopsies on patients aged 77

showed that the cause of death in 36 per cent was relatetd to the circulatory system; in 24 per cent to the respiration; and in only 13 per cent to malignant disease.

Some ailments develop in old people as a direct result of winter, and others are more difficult to bear in winter than in the summer months. A wise doctor will lead his elderly patients to understand that he knows the hard facts of existence, but that theirs is the benefit if they find the spirit to carry on.

Social and Medical Amenities for the Aged.

WILLIAM BARR. *The Medical Officer,* London, 76, No. 20:220-221 (November 16), 1946.

That the problem of assistance of the aged will be a growing one seems obvious with the present trend of population towards an increasing percentage of old persons. In 1931, one in ten of the population in Great Britain was aged (women over 60 and men over 65). By 1961 it is estimated that there will be one in six, and according to Beveridge, there will be 20 per cent in 1971. The care of the aged, however, is not easy of solution as there is no one group apart from the fact of age.

Temperamentally, old people feel important as they have every right to do, and they cling to their independence and individuality. As the majority of aged persons are relatively healthy and, within limits, able to look after themselves, the provision of suitable housing is a main step in planning for their care. In 1938, of all the houses built in Great Britain since the first world war, only 1 per cent of the dwellings provided since 1919 were specifically designed for old people who, at that time, constituted 10 per cent of the population. It is estimated that now 10 to 15 per cent of houses should be for the aged.

Whilst old age may be comparatively healthy, there is in many an element of slight absence of health exemplified in small departures from normal well-being, such as indispositions, or a certain amount of neglect and uncleanliness due to hindrance through rheumatism and the like. In such cases it would be desirable to have the services of a home helper or nursing orderly. With advent of illness of not too serious a character so as to make removal to a hospital unnecessary, help of this nature, together with the skilled help of the district nurse would go far to circumvent the tragedy of breaking up a home, and thus remove or lessen one of the fears of increasing age.

Despite all the outside attention that can be given to old persons, the time may come when institutional care is the only solution. The following is a résumé of the suggestions that have been put forward: easy transportation to and from hospitals; no large dormitories, rather single and double bedrooms; comfort and amenities, such as wireless, library and warmth, plenty of light and a garden; the aged people to wear their own clothes if possible; freedom to go out and about; encouraging visitors; occupational and diversional therapy, and personal services, such as letter writing.

There are, however, the "chronic" cases for whom continuous hospital treatment is necessary, ranging from those requiring only general care to those sick in body and mind, suffering from incontinence, crippledom, mental derangement of various forms, and all kinds of physical disorder. For these the need for efficient doctoring and nursing, just as in the acute wards is becoming more and more recognized. No one should ever be regarded as beyond remedy until there has been a thorough examination and investigation of all circumstances. Even then, skilled medical attention should still be the aim, for it is a policy of despair to make any line of demarcation between the acute and the chronic.

Carcinoma of the Prostate.

FLETCHER H. COLBY. *The New England Journal of Medicine,* 234, No. 17:560-563 (April), 1946.

A wave of enthusiasm for castration in all cases of prostatic cancer followed the early reports of Huggins and Hodges over four years ago. Since that time a great many papers on the effects of castration and estrogen therapy on the malignant prostate have appeared. Although there is still no uniform opinion on the best method of treating this disease, there is a tendency toward agreement in certain points. Castration and estrogen therapy have obviously been more effective in immediate beneficial results than has any other treatment previously employed. The use of external and interstitial radiation has greatly decreased, and partial removal of obstructing tissue by perineal operation has been largely abandoned in the treatment of prostatic cancer.

At present the question has arisen as to whether castration or estrogen therapy is the better procedure, and under which conditions these measures should be instituted. There is fairly general agreement that the radical operation of Young, consisting of total perineal removal of the carcinomatous gland, including the capsule, prostatic urethra, bladder neck and seminal vesicles, is the only method offering any expectation of cure. However, in this case it is important that the cancer should not have spread beyond the prostatic capsule, or at the most the lower ends of the seminal vesicles.

Belt reports 58 per cent of five-year cures of early prostatic cancer treated in the above manner; Young 53 per cent; Colston 50 per cent; Kearns, Kahle et al. and Marquart and Flaherty favor estrogen therapy. Kearns treated 37 patients with stilbestrol and he reported improvement of 30.

From a study of 1,000 cases at the Mayo Clinic made by Bumpus in 1926, the average survival period was thirty-one months after diagnosis. The improvement in life expectancy resulting from newer methods is shown in the report of 1944 by Nesbit and Cummins who treated 75 patients by orchidectomy. One-third died, and two-thirds were alive 21 months after the intervention. Eighty-four per cent of patients with metastases passed the nine-month period after the operation, during which Bumpus in 1926 had reported a survival rate of only 33 per cent. Eighty-seven per cent of patients without metastases were alive after 21 months. as contrasted with a survival rate of only 42 per cent after one year in the Bumpus series.

Nesbit and Cummins state that the maximum benefit to the patient is derived by delaying endocrine treatment until the onset of symptoms from advanced or metastatic lesions has occurred. Herger and Sauer expressed the opinion that orchidectomy preceded or followed by treatment of stilbestrol does not offer any advantages over castration alone. There appears to be no definite evidence that castration or estrogen therapy prevents metastases.

In cases of renal calculi with multiple small stones, the coagulum technique, in which fibrinogen solution is converted into a fibrin clot by adding thrombin has been employed successfully. Air pyelograms assist in determining whether or not this method is suitable. Although the procedure has limitations, it has considerable value, and the trauma to the kidney is minimal.

Bibliography of 26 references.

A Brief Survey of Prostatic Surgery.

C. D. CREEVY, *Minnesota Medicine*, 29, No. 10: 995-998 (October), 1946.

The demand for surgical treatment of obstruction of the vesical neck has increased manyfold in recent years, partly because the number of men living past the age of sixty has nearly trebled in the past half century, and partly because modern surgical operations upon the prostate gland have so reduced the risk and discomfort that patients have lost much of their dread of the procedure.

Excess of androgens, oversupply of estrogens, or increase of prolans from the anterior pituitary may be the cause of benign hypertrophy of the prostate gland.

The first deliberate operations aimed at the prostate gland were done through the urethra. Pare in 1575, Guthrie in 1835, and Mercier and Civiale in 1856 all devised instruments to incise the gland and excise bits of it. Bottini devised cautery for this purpose in 1873, however, the results were so uncertain, since the physician could not see what he was doing, that their use was abandoned. It is believed that the first deliberate open operation of this type was the perineal morcellation of a carcinoma by Billroth in 1867. Since then great improvements have been made, so that the urological surgeon has now three types of operation available in prostatism; suprapubic, perineal and transurethral. Irrespective of the type of prostatic operation to be done, careful attention must be given to the general condition of the patient, particularly as concerns degenerative diseases (cardiovascular disorders, diabetes). One must remember that the patient may dehydrate himself in an effort to reduce the frequency of urination or to prolong the interval between catherizations. Patients with impaired renal function may lose their appetites and develop vitamin and other nutritional deficiencies.

Another important consideration is the renal function. If the bladder is slightly impaired, a brief period of intermittent catherization with forced fluids may suffice to restore it to a satisfactory state. Inlying catheters are to be avoided, if possible.

When the patient is first seen, it is desirable to culture the urine; if needed, sulfathiazole should be used for Gram negative, and penicillin for gram positive organisms.

Spinal anesthesia is used in all cases, unless specially contraindicated. Bilateral vasectomy is done routinely before prostatectomy is started.

As soon as the patient is in position on the table, a drip of 10 per cent glucose in distilled water is started intravenously; it aids in maintaining the blood pressure, replaces fluid lost and promotes diuresis. It may prove desirable to use a 5 per cent solution of glucose rather than plain water as irrigating fluid.

In transurethral resection, careful electrocoagulation of bleeding points is essential; one should not depend upon traction on an inflated bag in the prostatic fossa, except in case of dire necessity.

In suprapubic prostatectomy, the author prefers to insert a pack of vaseline gauze into the prostatic cavity after large individual spurters have been controlled by suture. In perineal prostatectomy one can ligate individual bleeders; this is one of the best features of this operation.

In postoperative care, free, unobstructed drainage of urine is of paramount importance. The author uses a two-way hemostatic bag catheter (Foley-Alcock) with a continuous drip of sterile 0.5 per cent saline. A size 24 Foley catheter with a 30 c.c. bag is ordinarily used after perineal prostatectomy; a size 32 or 34 mushroom catheter makes a satisfactory suprapubic tube after suprapubic operation.

Out of the Joint...

. . . goes Arthritic Inflammation in a surprising number of cases

with ARTHRITIS VACCINE (CUTTER)

(Sherwood's Formula)

More than anything else, your arthritic patients need hope! And you can give it to them—with Cutter Arthritis Vaccine (Sherwood's Formula).

No one claims the vaccine is a cure—or that it will help all patients. Nor can Cutter say, definitely, just how Sherwood's Formula goes about alleviating arthritic pain.

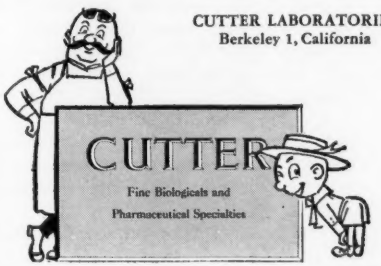
The fact remains, however, that suffering *is* reduced—and the progress of the disease seems to be slowed down in a large enough proportion of cases to make its trial worthwhile.

Cutter Arthritis Vaccine has shown up well in comparative clinical series with other arthritis therapy, including gold, without the latter's disadvantages.

Formula—polyvalent strains of:

Streptococci . . .	30%	with 1,000,000 organisms per cc.
Staphylococci . .	30%	
Pneumococci . .	10%	
M. catarrhalis . .	10%	
B. friedlanderiae .	10%	
B. influenzae . .	10%	

Order a supply of Arthritis Vaccine from your pharmacist. Or write to Cutter Laboratories, and we will be happy to send you a 5 cc. stock vial (enough for several weeks' treatment) for your own clinical trial.



CUTTER LABORATORIES
Berkeley 1, California

Postoperatively, fluids should be given intravenously in sufficient quantity. If the output is low in relation to fluid intake, urea nitrogen of the blood must be checked; the cardiovascular apparatus should not be overloaded by excessive fluid intake.

The risk of life is greatest from suprapubic prostatectomy, averaging about 8 per cent; however, since invention of the sulfa drugs and penicillin it has decreased. The mortality of perineal prostatectomy is low but the incidence of urinary incontinence is too high to justify its routine use. Transurethral resection shows a mortality of only 2 per cent.

Estrogens in Cancer

E. C. Dodds, London. *Schweizerische Medizinische Wochenschrift,* 76, No. 37/38: 842-843, 1946.

The treatment of prostate cancer with estrogenic substances was described for the first time in 1941 by Huggins and his collaborators. These authors observed that administration of synthetic estrogenic substances rapidly ameliorated local and general symptoms in cases where castration had no effect. In some cases, primary and metastatic tumors were greatly diminished.

The observations by Huggins have been confirmed by numerous American and British workers. Many patients who were bedridden with cancer of the prostate have been able to arise and to resume their work after treatment with estrogenic substances. However, according to American reports, this effect could not be maintained in all cases, because the treatment was interrupted prematurely.

Some side-effects of estrogen therapy are: meteorism, painful breasts, nausea, vomiting and pain in the testicles. However, these effects are not serious enough to have to interrupt medication because the success of the therapy overshadows its inconveniences.

The average dose employed is from

NOW a palatable protein hydrolysate with B-complex vitamins

The formula of Nitrolysin "Rorer," containing all the essential amino acids, explains its high potency. Its palatability enlists the co-operation of the patient, and helps to assure maximum clinical response.

Formula Nitrolysin contains natural enzymatic protein digest or hydrolysate derived from yeast and soya (including amino acids and B-complex vitamins) approximately 60%; added carbohydrate (sucrose) approximately 30%. Supplied either plain or flavored in bottles containing 250 grams. Write for professional information and tasting sample.

NITROLYSIN

Be sure your ℞ *specifies "Rorer."*

WILLIAM H. RORER, INC. RORER Est. 1910

Drexel Building, Independence Square
Philadelphia 6, Pennsylvania

FACTS for doctors and dietitians on special diets in which the use of an enriched, easily prepared cereal of high nutritive value is indicated.

Is there an ideal cereal for the aged?

A NEW and increasingly important field of interest to physicians is Geriatrics —the study of diseases, processes and special problems of the aged and aging. As the study and knowledge of Geriatrics expand, particular attention is being given to the dietary requirements of the aged. Investigations into this specialized field now indicate that foods combining the advantages of high nutritive value and thorough digestibility are increasingly important in the regimen of many older people, including those in normal health as well as those suffering from certain digestive disorders and degenerative disabilities.

"Enriched 5 Minute" Cream of Wheat offers such advantages in the form of a bland, tempting cereal that older people find most enjoyable. This cereal contains a high and effective source of Iron, and contributes generously to the carbohydrate requirements of the body. In addition, it supplies whole wheat amounts of Vitamin B_1, plus useful quantities of Calcium and Phosphorus and Niacin Vitamin. One part "Enriched 5 Minute" Cream of Wheat combined with four parts whole milk also supplies an appreciable amount of protein comparable in quality to the proteins of meat.

"Enriched 5 Minute" Cream of Wheat cooks to thorough digestibility after only 5 minutes of boiling.

The unusual combination of high nutritive values and low crude fiber content (one part in 200) is another factor in favor of this cereal as a dietary staple for older persons.

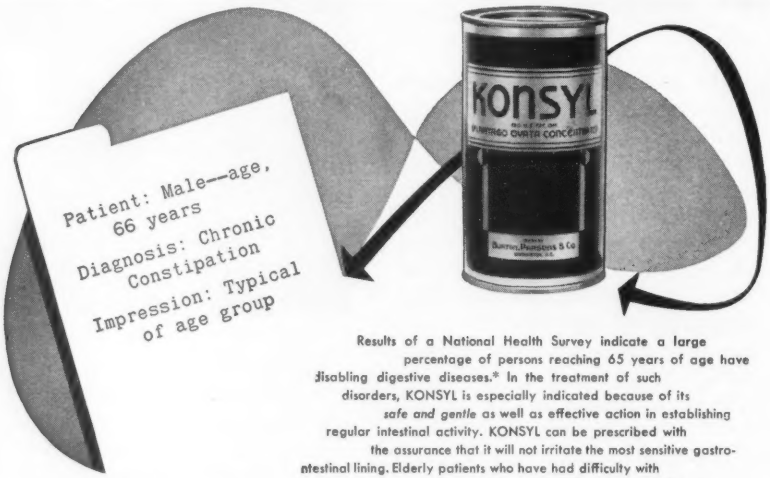
NOTE. For free booklet on use of "Enriched 5 Minute" Cream of Wheat in infant feeding, diets for expectant mothers, diets for the aged and bland diets, plus free sample package of the cereal (4-6 servings), write: The Cream of Wheat Corporation, 714 Stinson Boulevard, Minneapolis 13, Minnesota.

1 to 5 mg. daily; exact posology depends upon the amelioration of the symptoms and upon an analysis of the serum phosphatase.

The exact action of estrogenic therapy is unknown, nor do we know if estrogens act by suppressing the action of androgens. Also, it is impossible to ascertain if they are useful in treating other types of cancer so long as we are not better informed on these actions. Only a few successes in mammary cancer have been described until now.

In Great Britain the "Royal Society of Medicine" and the "British Cancer Campaign" have created a committee whose purpose it is to study the action of estrogenic substances in as great a number as possible of cancer patients.

Bibliography of 15 references.



Results of a National Health Survey indicate a large percentage of persons reaching 65 years of age have disabling digestive diseases.* In the treatment of such disorders, KONSYL is especially indicated because of its *safe and gentle* as well as effective action in establishing regular intestinal activity. KONSYL can be prescribed with the assurance that it will not irritate the most sensitive gastrointestinal lining. Elderly patients who have had difficulty with bowel-movements for several years will find sharp relief in the easy, well lubricated evacuations KONSYL treatment will afford them. Send for a free professional sample today and test the benefits of KONSYL in your own practice.
*Source—U. S. Public Health Service Survey showed 22.8%

MANUFACTURERS OF
L. A. FORMULA
CONTAINING LACTOSE, DEXTROSE AND PLANTAGO OVATA CONCENTRATE

Burton, Parsons & Co. 1515 U ST., N. W., WASHINGTON 9, D. C.

Glyco - HCl
(Pronounced gly-ko aitch see ell)
Effective HCl replacement therapy in achlorhydria and hypochlorhydria.
Bottles of 50, 100, 500 capsules for clinic prescription and private use.
Physicians' sample on request.
Burnham Soluble Iodine Co., Auburndale 66, Boston, Mass.

WHEN MIDDLE AGE BRINGS
A LET-DOWN IN GASTRIC EFFICIENCY

"We found a steady drop in acidity with advancing age."[1]

"Gastro-intestinal symptoms occur more frequently than any other symptom in patients over 40."[2]

". . . almost half the patients between the ages of 30 and 60 years included among their complaints that of dyspepsia."[3]

increased awareness of the prevalence of gastric secretory deficiencies in the middle aged and aging has focused new interest on the value of adequate replacement therapy.

FOR GASTRIC HYPOSECRETION

GASTRON

Effective substitution therapy for deficiencies in gastric secretion, Gastron increases the acidity and peptic activity of gastric contents . . . improves gastric digestion . . . promotes normal emptying time . . . relieves epigastric distress.

GASTRON is a physiologic mixture of gastric enzymes and hormones plus hydrochloric acid in a palatable, alcohol-free medium . . . contains: **pepsin, rennin, secretin, mucin, and the antianemic principle.**

INDICATED in gastric hyposecretion... gastritis associated with achlorhydria; anacidity and achylia in the middle aged and aging; hypochlorhydria associated with food allergies and nutritional deficiencies, including the anemias.

THE USUAL DOSE is 2 to 4 teaspoonfuls diluted with 1 or 2 volumes of cold water, following each meal.

SUPPLIED in bottles of 6 and 32 fl. oz.

1. Meyer, Spier, and Neuwelt: Arch. Int. Med. 65:171, 1940

2. Kopelowitz: J. Missouri M. A. 38:55, 1941

3. Rivers: Proc. Staff Meet., Mayo Clin. 13:87, 1938

Originated by FAIRCHILD BROS. and FOSTER

Frederick Stearns & Company, Division of Sterling Drug Inc.

DETROIT 31, MICHIGAN New York Kansas City San Francisco
Windsor, Ontario Sydney, Australia Auckland, New Zealand

Trade Mark Gastron Reg. U. S. Pat. Off.

Better Nutrition FOR A Brighter OLD AGE

Gerilac —a new dietary supplement for the aged . . . a very practicable solution to the problem of achieving dietary balance in older patients.

Gerilac supplies in one reliquefied pint at least one-third of the daily dietary protein allowance* *plus* valuable milk carbohydrates. It also provides a full allowance of vitamins and minerals. GERILAC is palatable, convenient to prepare and easy to digest.

Gerilac is well suited in all ages for use as a beverage, with or without flavoring. It can also be used in special diets as a basis for milk dishes. Particularly valuable in convalescent and pre- and post-operative diets in all ages.

Write for Professional Literature.

Borden's

*Based on the latest recommendations of the National Research Council.

PRESCRIPTION PRODUCTS DIVISION
350 MADISON AVENUE, NEW YORK 17, N. Y.

NET WT. 1 LB.
Gerilac
MODIFIED MILK FOR SPECIAL DIETARY USE
Spray-dried whole milk, skim milk, dried brewer's yeast (source of B vitamins) fortified with riboflavin concentrate, vitamin A and D concentrate from fish liver oil, irradiated ergosterol (vitamin D), ascorbic acid (vitamin C), niacinamide, monosodium phosphate, and iron citrate.

Gerilac *-A Dietary Supplement for the Aged.* GERILAC *contains spray-dried whole milk and skim milk and is fortified with vitamins A and D, B-complex, C, together with niacinamide, monosodium phosphate and iron citrate. At pharmacies in 1-lb. tins.*